AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 29 OCTOBER, 1946 NUMBER 10

A STUDY OF LEWISITE LESIONS OF THE EYES OF RABBITS

IDA MANN, A. PIRIE, AND B. D. PULLINGER
London and Oxford, England

The effects of mustard gas when applied to the rabbit's eye by various methods have been set out in a previous publication.[1] We consider it of interest to describe a parallel series of experiments using Lewisite (β-chlorovinyl-dichlorarsine), since the actions of the two chemical-warfare agents appear to differ in all important points. This is only to be expected, for mustard and Lewisite react largely with different groups in the protein molecule, and the difference in the pathologic changes in the eye lesions probably reflects this fundamental difference.

The characteristics of mustard-gas lesions may be briefly summarized as follows:

1. Application is not painful, and symptoms do not appear for some hours.
2. The pupillary reaction is not affected.
3. Perforation and loss of an eye are caused only by relatively large doses (0.005 c.c.), and even then are long delayed. Perforation never occurs as a primary lesion before the stage of vascularization.
4. Vascularization never occurs unless the limbus is damaged by the mustard (that is, purely corneal lesions do not vascularize).
5. Vascular lesions do not all perforate; they tend to be chronic, to relapse, and to show intracorneal hemorrhages from newly formed vessels, which latter are of peculiar and characteristic form.
6. Cholesterin and other lipoid scars follow some vascular lesions, and subsequently these tend to break down[2] (delayed mustard-gas keratitis).
7. Edema of conjunctiva and cornea is present, but not excessive.
8. Iris and ciliary body are relatively little involved. There is no late effect on pigment.
9. Characteristic vessels form in cornea and conjunctiva.

In the case of Lewisite we shall show that:

1. The action is immediate and painful.
2. There is an immediate strong miotic action.
3. Perforation and loss of an eye are caused with relatively small doses (0.001 c.c.); perforation may occur within a few days without vascularization, or later after the entry of blood vessels.
4. Vascularization is independent of the site of the primary lesion; it occurs when a sufficient dose of the Lewisite reaches either the cornea or the limbus.
5. All lesions run a definite course to recovery or destruction; not all vascular lesions perforate; there are no relapses and no recurrent hemorrhages.

6. Cholesterin and other lipoid scars do not occur, and there is no late breakdown due to them. The end result of a nonperforating severe lesion is dense fibrous scarring with pigment proliferation on the corneal and conjunctival epithelium.
7. Edema of the lids and conjunctiva is immediate and severe; edema of the cornea is extreme with all but the smallest doses.
8. Involvement of the iris and ciliary body is early and severe, followed by gradual depigmentation and shrinkage of the iris stroma.
9. The corneal vessels do not show the characteristic varicosities of mustard vessels. They are straight and evenly and radially arranged. No characteristic vessels appear in the conjunctiva.

These conclusions show that Lewisite has a much more destructive and extensive effect than mustard gas. It is much more difficult, therefore, to produce minimal lesions and, indeed, this can be done only by means of short exposures to vapor, whereas in the case of mustard gas, minimal lesions can be obtained with liquid.

The clinical report which follows is based on observations of lesions of varying severity obtained by treating 27 rabbit eyes with varying amounts of Lewisite vapor or liquid. The lesions are classified according to severity. "Very mild" and "mild" lesions are those which (after short exposures to vapor) recovered without passing through a stage of corneal vascularization. "Severe" lesions (produced by longer exposure to vapor) recovered with slight permanent scarring after partial vascularization. In "very severe" lesions, the eye was lost by shrinking and corneal scarring with or without perforation.

Experimental procedure

Animals used. A variety of rabbits was used, including black, with dark-brown eyes; crossed Dutch, with blue eyes; some with gray, and some with heterochromic eyes. The animals with blue eyes were used to study the effect on iris vessels, since dilatation of vessels and small hemorrhages can be most easily seen in them; those with brown eyes were used to study depigmentation of the mesodermal pigment of the iris; and those with either blue or brown eyes could be used in the observation of proliferating limbal conjunctival pigment, since both types have limbal pigment rings in most individuals. Albino eyes are not suitable, as they are very difficult to observe accurately during life; moreover, many of the reactions seen in pigmented rabbits do not occur in the albino. Twenty-seven experiments were performed.

Method of application of Lewisite. Three different methods of application were used.

1. The rabbits were anesthetized, and the lids held open. The center of the cornea was exposed to Lewisite vapor obtained from cotton-wool pledgets soaked with Lewisite inserted into the open ends of glass tubes of varying sizes. The tubes were then held over, but not in contact with, the part of the eye required, for varying lengths of time. The dosage was impossible to standardize, but a series of "very mild" and "mild" lesions was produced.

2. The rabbits were anesthetized, and small glass applicators, similar to those described in our mustard experiments, were used. They delivered between 0.1 mg. and 0.2 mg. of liquid Lewisite, as determined by arsenic estimations. The lids were held open, and applications made to the cornea or the limbus, as re-

quired. "Severe" lesions were produced in this way.

3. Unanesthetized rabbits were used with the same applicators as in method 2, but the rabbits were allowed to blink so that the liquid was immediately spread out and involved cornea, conjunctiva, and lids. This type of lesion simulates that likely to occur in persons exposed to Lewisite spray.

Experimental results

Group I.

Very mild lesions. Ten eyes were examined. All the injuries in this group were produced by vapor, and the rabbits were anesthetized, so that it is not known whether exposure to Lewisite vapor is painful in rabbits.*

At the time of application the eyes were observed for 15 minutes, and at frequent intervals after that. During the first 15 minutes, there was no conspicuous change in the corneal epithelium, except that it showed slight pitting due to exposure, and occasionally appeared faintly grayish. In 15 minutes, isolated hydropic cells began to appear in the epithelium. These increased to a definite bedewing in 1½ hours. The pupil did not contract, but the iris vessels flushed in most eyes within 5 minutes; in one rabbit in 3½ minutes. Lacrimation was variable, but usually appeared in from 6 to 10 minutes.

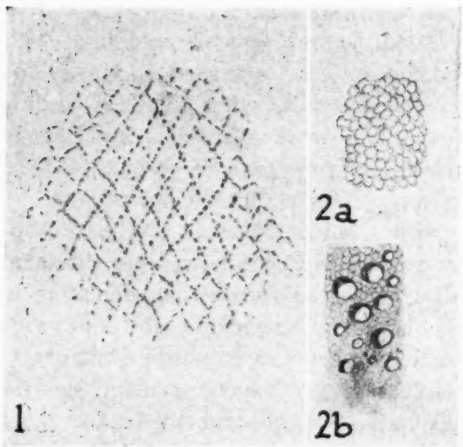
In 1½ hours, or less, the exposed area revealed a fine punctate staining with fluorescein. This increased in density for approximately 7 hours and then became less. It had practically disappeared at the end of 24 hours and, in all eyes, cleared up completely within 36 hours.

Slight mucopurulent discharge appeared, derived especially from the third lid, which became somewhat edematous in 2¼ hours. This edema and discharge cleared up in all eyes within 36 hours.

Interesting changes occurred in the substantia propria and the endothelium in these very mild injuries. They were observed in detail with the slitlamp. Within an hour, the corneal corpuscles could be recognized in direct illumination much more easily and over a wider area than normal. They appeared to be swelling, but were not opaque (that is, not visible by retroillumination or sclerotic scatter). The endothelium, however, in about half the eyes showed a widespread and peculiar change, the cells swelling up and producing a series of faint linear ridges arranged in a diamond pattern, easily visible by retroillumination (fig. 1). It was possible to watch the development of this diamond pattern, which formed quite rapidly at the end of the first hour, taking about 10 minutes to become complete.

During the same time, irregularities of the epi- and endothelial surfaces were seen forming in the zones of specular reflection. These appearances were transitory, lasting from 2 to 3 hours to a day, not seen in every case, and gradually being replaced by a condition of uniform swelling of every endothelial cell. This swelling was much greater than ordinary "endothelial bedewing" and was easily visible all over the cornea (fig. 2). When it subsided, large Hassle-Henle bodies sometimes appeared. It began to subside

*Judging from the sensations of two human beings exposed to extremely small concentrations of Lewisite and of ethyl dichlorarsine, respectively, a stinging sensation is felt immediately, and it would be almost impossible to keep the eyes open for anything like the time needed to produce a serious corneal lesion. In respect of sensory irritation, Lewisite vapor differs conspicuously from mustard gas, and the risk to the eyes from vapor might, therefore, be small, in spite of its much more violent action. The main risk would be from the the entry of a single droplet, such as was used in the third set of experiments.



Figs. 1 and 2 (Mann *et al.*). Fig. 1, Diamond pattern on the endothelium seen by retroillumination. Fig. 2a, Edema of endothelial cells —very gross bedewing. 2b, Hassle-Henle bodies formed after healing.

in 3 days and had gone in 5 days, or less. The swelling of the corneal corpuscles sometimes continued. They became increasingly easily visible, being seen not only by direct illumination, but soon (24 hours) by retroillumination as well, and in two days presenting a characteristic appearance. They were then very swollen, fluffy, and opaque, and could be seen by light scattered within the cornea (corneal or sclerotic scatter), as well as by retroillumination. A profound change had occurred in them which completely altered their physical properties, including their index of refraction. They will be referred to as "opaque corneal corpuscles." They appeared through the whole thickness of the cornea (fig. 3).

At the same time, the surface layers of the substantia propria became split apart and edematous, but in these very mild lesions the stratification did not extend deeper than the superficial quarter and might not even occur. It reached its maximum in 3 to 4 days and then subsided rapidly, within the next 24 hours, disappearing by the 5th day.

The changes in the iris might not progress beyond the initial hyperemia, which subsided in 24 hours. In some eyes, however, although no aqueous flare was observed, a small amount of deposit, possibly fibrinous, was seen on the endothelium on the fourth day. In no case was

Fig. 3a (Mann *et al.*). Opaque corneal corpuscles seen by sclerotic scatter and in the narrow beam of the slitlamp. In a central Lewisite vapor lesion. Those in the center of the lesion are completely destroyed, those at the periphery are all opaque. Farther out they are more scattered.

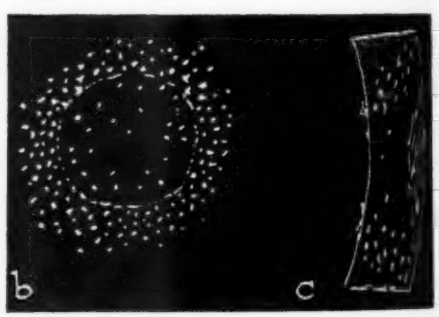


Fig. 3b (Mann *et al.*). In a minimal lesion, showing as in fig. 3a, destruction of the central cells and opacity of those around the periphery. Fig. 3c, The lesion in b in the narrow beam. Note funnel-shaped arrangement of opaque corpuscles, edema of surface layers of substantia propria and endothelial deposits.

any alteration in the color of the iris seen in either blue- or brown-eyed rabbits, nor was there any disturbance of uveal pigment or of the lens capsule.

The fate of the "opaque corneal corpuscles" requires histologic investigation for its complete elucidation, but with a slitlamp certain changes were observed. It was possible by directing the vapor towards the center of the cornea to produce a localized circular lesion. The circumference of the circle on the first day showed large numbers of these opaque cells (fig. 3). Within this ring, there was a narrow clear zone. In the center of the circle, the superficial layers of the substantia propia were edematous, and the deeper layers contained remnants and debris of cells, with perhaps a few opaque cells in the deepest layers only. The opaque condition of the cells appeared to be an intermediate one between normality and complete destruction. This appearance continued for 3 or 4 days and then, in the zone of opaque cells, very fine short processes were made out in connection with some of the cells. These fine processes increased in size and in number, and the cell bodies became less visible.

From the 5th to the 8th day, the ring was slowly transformed from a ring of opaque cells to a circular zone of long silky fibrils (fig. 4). These were seen progressing towards the center of the circle, which then looked clear and almost normal, though it contained some opaque cells. By about the 12th day, the whole lesion was transformed into a patch of fine silkiness. This appearance slowly faded, and no trace of the lesion was finally left. In one case the cornea was completely normal in 9 days; in others, faint silkiness could still be detected in a month. In most, no trace of any abnormality could be found in 6 weeks.

This type of lesion is, therefore, characterized by very transient conjunctival and iris irritations and by damage to corneal corpuscles. Some kind of repair is effected, possibly originating in the partially damaged corneal corpuscles.

GROUP II.

Mild vapor lesion. Two eyes were examined in this group. They were not very different from the lesions in Group I, except that they were more severe and longer in clearing up. Their characteristic

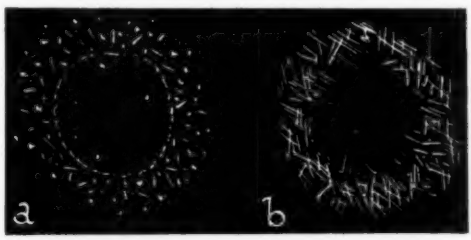


Fig. 4 (Mann *et al.*). Changes in the opaque corneal corpuscles: a, At the 5th day they are seen to be elongating. b, At the 8th day they are transformed into a ring of silky fibrils.

was a short period of intense edema of the cornea, with increased activity of the limbal blood vessels, which appeared about to enter the cornea and then retrogressed. The contraction of the pupil, which will be seen to be characteristic of the next group, occurred in the worse of these two mild lesions.

The course of events in this eye is typical. A grayish patch was seen almost immediately on the epithelium. The pupil contracted, and the iris began to flush within half an hour. The typical diamond pattern appeared on the endothelium in an hour, when the smallest iris capillaries were also dilating. In 2 hours and 20 minutes, the eyelids looked pink, and the third lid showed slight edema. The edema of the substantia propria was beginning. Slight discharge appeared later, and at 5 hours and 40 minutes, the epithelium over the point of maximum exposure had sloughed off, and the edema of the substantia

propria had considerably increased. At the end of 24 hours, the cornea looked "steamy" and was too hazy for any details of iris or anterior chamber to be seen. In 2 days the cornea was intensely swollen, an aqueous flare could be seen, and the eye looked worse, though there was no more discharge. The cornea was very much increased in thickness, was waterlogged, and appeared to be split into two layers: a superficial layer—very edematous and pale blue in color, with wide separation of the fibrils—and a deeper, more dense and homogenous layer, of a more yellow color (fig. 5). The appearance was peculiar and characteristic, the eye seeming to bulge, the contour of the cornea being almost conical, and the eyes looking rather like moonstones and definitely bluish in color. The term "moonstone eye" was coined to describe the condition. This continued for 5 days, when the limbal blood vessels became active and a few superficial loops crossed the limbus on to the cornea. The iritis had, however, subsided completely, leaving two small posterior synechiae and a fibrinous deposit on the endothelium.

In 6 days, the vessels disappeared, the edema started to subside, and the eye to improve rapidly, so that in 15 days it appeared perfectly normal to macroscopic examination. The slitlamp, however, showed a fine silkiness which persisted in its densest part for 5½ months and may be permanent. It is, however, too slight to interfere with vision, and the eye may be considered normal.

This rabbit showed in a minor degree the edema which is so characteristic of the more severe lesions.

GROUP III.

Severe vapor lesion. Three eyes were examined in this group which showed partial recovery with fair function, after vascularization. At the time of application, the corneal epithelium became grayish, and the pupil contracted strongly. The early changes were similar to those in Group II; namely, changes in the epithelium and endothelium, and flushing of the iris. The diamond pattern appeared on the endothelium in half an hour, and edema of the superficial layers of the substantia propria was also beginning at that time. An aqueous flare was noted at 2 hours. All the changes began slightly earlier and were more evident than in Group II. The substantia propria began to split into layers at 4 hours, and the edema was advanced in 24 hours, so that the cornea had a distinct opalescent appearance and was almost at the moonstone stage.

At 24 hours, there was a staining area in the center of the cornea, corresponding to the region of epithelial destruction. The remaining epithelium and endothelium were heavily bedewed. The injected iris showed through the edematous cornea with a distinct universal red glow. There was an aqueous flare, and free cells were seen in the aqueous. A curious pattern of concentric circles of fine pigmented dots could be seen on the anterior surface of the lens capsule, probably a deposit from the aqueous of blood and pigment-containing cells. There was little or no discharge, although the conjunctiva was hyperemic.

In 2 days the corneas presented the typical moonstone appearance. They were swollen and bulging, bedewed and edematous, and no details of cells could be seen. The staining had practically gone. The iris still appeared bright red.

The moonstone appearance increased for 5 days and did not then subside, as it did in Group II. Instead, on the 5th or 6th day, the engorged limbal blood vessels began to invade the cornea around almost the whole circumference simultaneously. These vessels were both super-

ficial and deep. The deeper ones were larger and sent out more branches than the superficial ones; but all of them were straighter, of more even caliber, and more regular arrangement than those seen in a mustard-gas vascularization. They were preceded by small intracorneal hemorrhages, which soon cleared up and did not tend to recur over long periods, as did those typical of mustard gas (fig. 6).

The vessels advanced for 14 to 18 days, growing steadily in from the limbus all around towards the center. As they advanced, they became very regularly arranged in a radial row of thin parallel channels of even caliber, lying in the superficial layers of the substantia propria. At their extending tips, they branched and formed a very rich capillary network, with a few detached ends and small hemorrhages only. They resembled the new vessels of granulation tissue much more than do those of mustard-gas vascularization, which do not end in a

FIG. 6

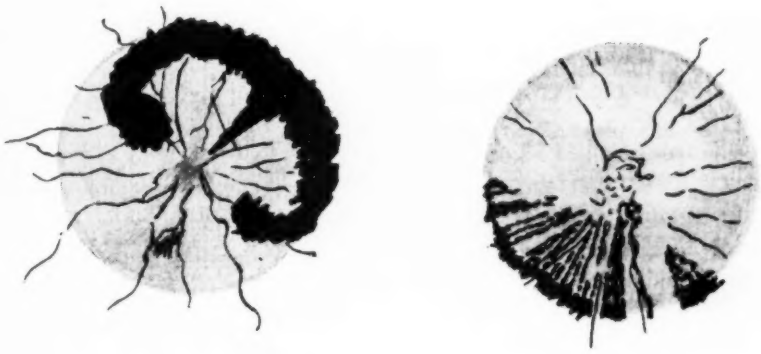


FIG. 12

Fig. 6 (Mann *et al.*). Vascularization: a, deep vessels; b, superficial vessels preceded by capillary hemorrhages; c, radially arranged superficial vessels. A deep vessel is seen near the top.

Fig. 12 (Mann *et al.*). Two scarred and shrunken eyes showing bizarre pigment proliferation.

capillary aborization, but as straight tips.

After 18 days, the edema began to clear rapidly, the vessels ceased to advance, became thinner, and the fine capillaries disappeared rapidly. The larger radial trunks also disappeared, except for a few of the largest ones.

In 3 weeks the edema of the substantia propria disappeared, the cornea returned to its normal thickness, although it still showed disturbance of endothelium (beaten-silver reflex), and there might be slight epithelial bedewing. The vessels were all narrow and empty, or showed slow and interrupted circulation only. The larger trunks alone were visible. As the edema of the cornea subsided, a fine silky change was seen all over it, similar to that seen in the other groups, although in Group III the excessive edema obscured the preceding stage of opaque corneal corpuscles. This fine silkiness slowly disappeared in about 6 months.

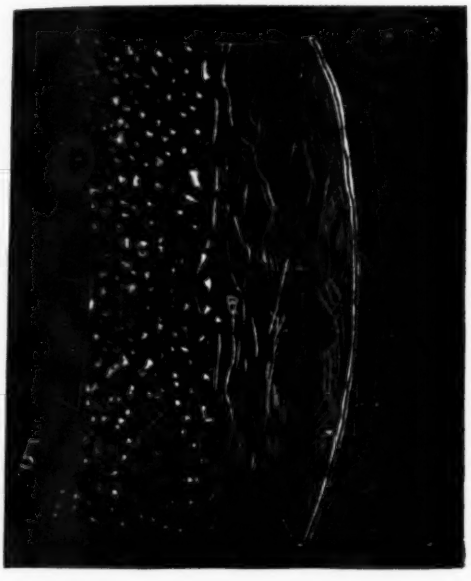
As the cornea cleared (after the 18th day), the iris again became visible. It was then seen that profound changes had occurred in it. Brown-eyed rabbits showed these changes best. At 18 days, or sooner, it was noticed that the iris, to macroscopic observation, no longer looked dark brown, as it was originally, or bright or dull red, as it was at the height of the reaction, but had become light blue. This remarkable change might involve the whole iris, but was most conspicuous in the circumpupillary zone over half the width of the iris or more (fig. 7). The blue patches might be circinate in outline, or confluent; in some eyes, only a narrow peripheral ring of brown was left.

If examined in more detail, the pupil was seen to be somewhat dilated, was irregular in outline, and possibly showed a few posterior synechiae. Here and there, usually above and below, there was considerable ectropion of the uvea, as though the dilated appearance of the pupil were due to contraction of the stroma. In some cases this was so excessive at one or two spots that the tips of the ciliary processes were pulled right around, so that they appeared at the edge of the pupil. The sphincter was not destroyed, since these distorted pupils showed a reaction to light. The stroma of the iris had undergone a peculiar change. In the brown zone at the periphery, the chromatophores appeared normal, bright brown, with long interlacing processes, and spread out in an even sheet. As the light-blue areas were approached, the chromatophores became darker in color, lost their processes, and resembled very dark-brown spherical and amorphous deposits, rather than cells. This withdrawal of processes was confirmed microscopically. The cells were thickly aggregated at the edges of the blue areas and were present all over those as isolated dark spots dotted over the unpigmented stroma. This stroma, exposed by the retraction of the chromatophores, appeared at the 18th day somewhat edematous and translucent. The vessel walls were easily seen and appeared normal. The stroma finally looked fluffy and atrophic and, at times, as if the surface layer had been torn off, leaving odd tags and fringes floating loosely attached. This change and the ectropion of the uvea appears to be permanent, having been observed for 8 months without further alteration. No change was observed in the ectodermal uveal pigment, other than ectropion. It was not depigmented.

These eyes appeared to have excellent function in spite of the residue of the severe iritis. The fundi were examined with an ophthalmoscope and appeared normal.

GROUP IV.

Very severe lesions. These lesions ended in loss of the eye. Twelve eyes



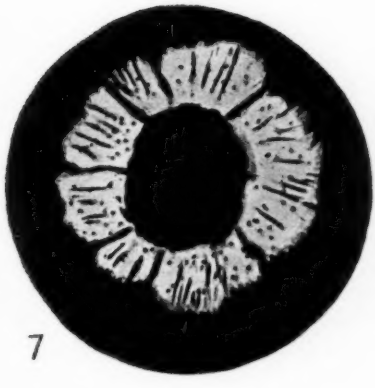


FIG. 5 (MANN ET AL.) THE WATER-LOGGED CORNEA OF A "MOONSTONE EYE" SEEN IN THE NARROW BEAM OF THE SLITLAMP; THE SURFACE LAYER IS BLUISH, THE DEEPER PART YELLOWISH.

FIG. 7 (MANN ET AL.) A BROWN EYE WITH CIRCINATE PATCHES OF DEPIGMENTATION AROUND THE PUPIL, AND SOME ECTROPION OF THE UVEAL MARGIN OF THE PUPIL

were examined. The initial sequence of events was similar, but more rapid and more severe than that seen in Group III. Some of the lesions in this group of 12 eyes were produced by a single droplet of liquid Lewisite; others were caused by exposure to vapor for varying times, up to 20 minutes. In some eyes the cornea alone was injured, in others the limbus, and in others again the cornea, limbus, lids, and conjunctiva were affected. Thus, some of the original injuries were more severe than others, although all the eyes were finally lost. The exact method of application did not appear to be important, except in those cases where the lids and conjunctiva were extensively injured, when the eye was lost in about half the usual time, and many of the stages of destruction were telescoped.

As a point of interest, it may be mentioned here that liquid Lewisite applied to the ocular conjunctiva increases the transparency of the sclera so that the uveal pigment shows through in 2 minutes as a black spot. This disappears within a day.

The eyes can be divided roughly into (a) those lost after initial vascularization and (b) those which perforated before vessels had entered the cornea.

(a) The course of events in an eye lost after initial vascularization was as follows: The site of application of the liquid or vapor became immediately opaque. When liquid was used the droplet showed no tendency to slide. It appeared to soak into the cornea almost instantaneously, the opaque area increasing in size by spreading concentrically for about two minutes. The Lewisite then reached the aqueous, where it diffused rapidly, the whole iris flushing, and the pupil contracting very quickly and strongly, so that in 2½ minutes, it was pinpoint in size. There was some secretion of clear tears but this was variable from rabbit to rabbit. In 5½ minutes there was a faint surface haze over the whole cornea. In 10 minutes, the conjunctival vessels were flushed. In 15 minutes, a severe chemosis of the ocular and palpebral conjunctiva was beginning, even in eyes in which the cornea alone had been treated. In those in which the conjunctiva was injured, it appeared sooner, but was otherwise similar. The areas involved stained only very faintly with fluorescein at this stage (fig. 8).

Fig. 8 (Mann *et al.*). Severe chemosis of ocular or palpebral conjunctiva 30 minutes after a droplet of liquid Lewisite entered the eye.

In half an hour the corneal epithelium had become so edematous that it was impossible to see any details of the iris. In 1½ hours, the epithelium was beginning to loosen and slough off, giving an almost universal stain with fluorescein. In 4 hours, or less, there was a watery discharge containing cells, and the chemosis had reached surprising proportions. The entire conjunctiva, ocular and palpebral, was enormously swollen, so that the lids were held right away from the eye, sometimes bulging more than half an inch. The cornea was overlapped by folds of gelatinous injected conjunctiva, the appearance of the eye being striking and peculiar. The swollen conjunctiva was covered with fine vessels, and small petechiae were seen to develop. The lymphatics were widely open and were easily observable

as clear, distended, optically-empty tubes in the narrow beam of the slitlamp (fig. 9). The corneal epithelium had nearly all sloughed off. There was edema of the substantia propia in its superficial fourth. Descemet's membrane looked corrugated, and the pupil was still contracted. In seven hours the petechiae had increased in number and size. The whole cornea stained. The edema involved nearly its whole thickness. No details of cells or of the anterior chamber were seen.

In 24 hours a remarkable improvement in the chemosis had occurred, but the eye was much worse. The lids were again in apposition to the globe. There was very little discharge. Large conjunctival hemorrhages had appeared. The whole cornea stained, and the stain reached the aqueous in 5 minutes.

The anterior chamber was now visible. It was full of strands of gelatinous exudate, forming large solid masses in the lower part. The circulation of the aqueous appeared to have ceased, as the green color of the fluorescein was unchanged in 6 hours and was only slightly diminished in 24 hours after application. In 2 days there was practically no discharge, but the cornea still stained and was more opaque. The surface of the iris looked an almost uniform blood red. At 3 days, there was an attempt at regeneration of the conjunctival epithelium from the limbus and, if this were pigmented, a pigment slide was seen. The staining was not quite complete.

At 4 days, there was no discharge, but the eye was slightly worse. At 5 days, there might be a somewhat moonstone effect as the corneal edema began to increase, but this stage of intense swelling was less the more severely the eye was damaged.

Between the 6th and the 8th day, vessels began to invade the cornea, usually first above and below, but soon equally all around. The center of the cornea still stained and became excessively swollen, unless the eye was very severely damaged. The vessels continued to grow in from the 6th to the 24th day, when they had almost reached the center. In a few eyes, this happened at the 20th day, or might be delayed for 34 days. The arrangement of these vessels was striking. They were long, straight, and radially arranged at right angles to the corneoscleral junction. They were excessively numerous and appeared to naked-eye examination almost like a sheet of blood. As they approached the center, the periphery of the cornea cleared somewhat, and the growing tips only showed as a bright-red ring which contracted as it advanced, appearing to push the edema ahead of it, so that the center of the cornea looked like a conical, blue projection in the center of a red circle. This central cone became smaller, and the contracting ring of capillaries was raised into a ridge of advancing granulation tissue, which finally reached the center and projected as a small knot or bleb. As this happened, the central parts showed a gradually diminishing staining area. Finally, the center of the cornea was cast off as a small slough. In some cases, this coincided with the arrival of the ring of granulations at the center, and there was no true perforation. Sometimes, on the other hand, the central slough separated before the vessels had reached it and a descemetocele, which rapidly perforated, resulted (fig. 10). In either case (granulation or perforation) the eye then rapidly shrank and the vessels narrowed and became less in number, but did not disappear. Perforation or separation of the central slough (fig. 11) might occur at any time from the 19th to the 34th day (earlier in the most severe lesions, as will be seen later). The eye then ceased to stain, shrank, and quieted to a condition of phthisis bulbi. A slight muco-

purulent discharge continued the whole time, varying from day to day, but not severe. In 1½ to 2 months, the shrunken eye became pigmented in parts. The limbal pigment ring proliferated, and large, dense, almost black masses of pigment grew on to the cornea in sector-

Lewisite produced necrosis of the cornea before the blood vessels had extended into it. Both lesions were produced by a large droplet. In one case, the rabbit was anesthetized; in the other, it was not anesthetized and was allowed to close the eye at once, thus spreading the Lewisite

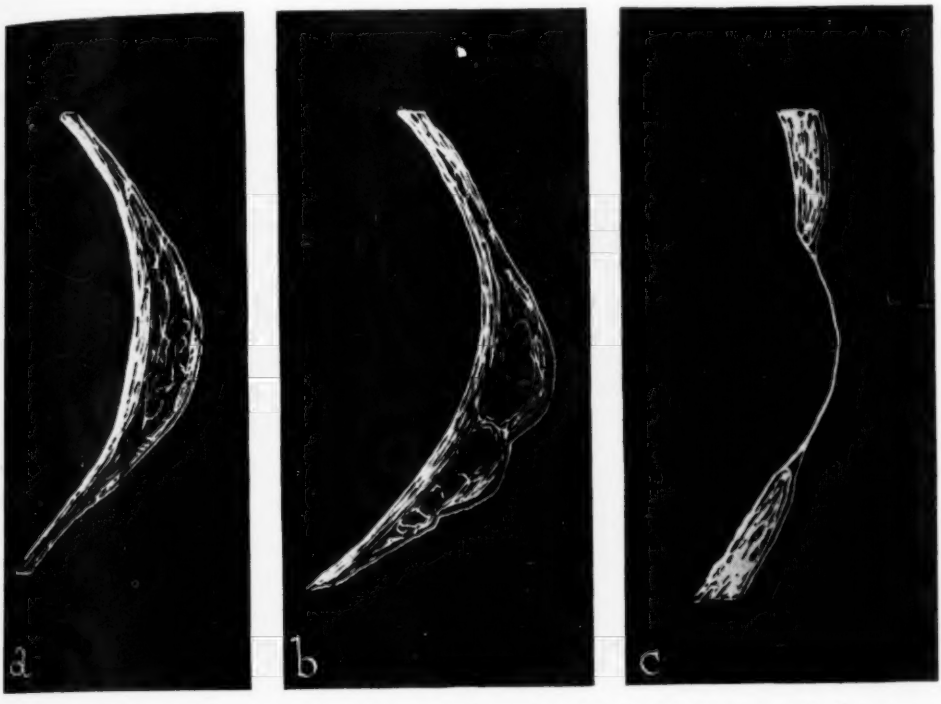


Fig. 11 (Mann *et al.*). Stages in the formation of a descemetocele, seen with the narrow beam of the slitlamp: a, severe edema; b, formation of large fluid spaces; c, perforation only closed by Descemet's membrane.

shaped fringes (fig. 12). The scarred eye became less vascular, and it was often possible to make out, here and there, traces of depigmented iris. There was usually an almost complete anterior synechia, and the pupil was filled with cyclitic membrane. Uveal pigment might be seen on the back of the remains of the cornea. The eye was useless.

(b) Severe lesions which perforate before blood vessels enter the cornea: In 2 eyes of the 12 in the series of very severe lesions the destructive action of the

all over the conjunctival sac. The sequence of events in this eye began with instantaneous intense spasm of the lids, followed by lacrimation in 20 seconds (at first clear tears; in 1 minute and 20 seconds, milky Harderian secretion). In 6 minutes, the third lid was becoming edematous and in 10 minutes, the lids themselves started to swell. The eye was kept closed with occasional blinks. In 20 minutes, the edema was so great that the lids were lifted off the globe and the eye could hardly be kept closed. In 3 hours,

it was not possible to see the cornea, and there were conjunctival petechiae. Lacrimation continued.

In 24 hours the edema was beginning to subside, and the eye was discharging mucopus. There was a violent iritis, and the cornea was edematous all over in the superficial third. The whole cornea stained. On the 3rd day, there was much discharge, and the lids were still swollen. On the 4th day, the lids were stuck together with discharge. There was severe iritis. The cornea was not very swollen.

Fig. 13 (Mann *et al.*). Brawny induration of the lids, discharge and sloughing of the cornea in a very severe Lewisite lesion on the 12th day.

The stain of the day before was still present in the anterior chamber. On the 8th day, there was hypopyon, and the lids were brawny and contracting down on the globe, so that the eye could not be fully opened. No vessels had entered the cornea, which was more opaque. In 10 days, the cornea was still avascular, very opaque, and covered with pus (fig. 13). On the 14th day, the center of the cornea appeared to liquefy and melt away, leaving a descemetocele which remained intact till the 26th day, when it ruptured, leaving only the remains of an eye in a mass of pus. No attempt at repair or vascularization took place. The lids and conjunctiva continued to shrink, so that by the 36th day all that could be seen was a narrow discharging palpebral aperture between lids adherent to a disorganized globe.

The course of the lesion in the other eye in this category in an unanesthetized rabbit was similar, the descemetocele appearing on the 12th day, when this rabbit was killed. Here again there was severe discharge.

These two lesions seem to show that widespread damage to the conjunctiva leads to persistent discharge, failure to vascularize, and to shrinking of the conjunctiva. In the rest of the "very severe" series, the conjunctiva was damaged, but never over so wide an area as in these two.

Many of the rabbits were watched for nearly a year and in no case, was secondary lipoid degeneration and cholesterin deposition observed, so that no condition similar to delayed mustard-gas keratitis was seen, nor seemed likely to occur. The eyes either recovered completely, showed stable scars, or were completely destroyed. The main points of interest were: (i) Peculiar effect on corneal endothelium and corneal corpuscles. (ii) Miosis. (iii) Intense, but transient, edema of lids and conjunctiva. (iv) Intense edema of the cornea, reaching a maximum after the lid swelling had subsided. (v) Characteristic type of vascularization. (vi) Involvement of iris and ciliary body with mesodermal depigmentation and shrinking, and ectodermal pigment displacement. (vii) Effects appear specific for total dose entering eye rather than for anatomical site of lesion.

Imperial Cancer Research Fund Laboratory.
Nuffield Laboratory of Ophthalmology.

TABLE 1

LEWISITE LESIONS OF VARYING SEVERITY IN 27 RABBITS' EYES

Very Mild	Mild	Severe	Very Severe	
No immediate change. Iris flushed in 5 min.	Pupil contracted in 2 min.	Pupil contracted, 2 min.	Contraction of pupil, 2 min.	
↓	↓	↓	↓	
Punctate staining in 1½ hrs. and increased visibility of corneal corpuscles and diamond pattern on endothelium	Diamond pattern in 1 hr. Slight edema of lids, 2½ hr.	Diamond pattern in ½ hr. and edema of substantia propria	Severe chemosis and complete corneal haze, 15 min.	
↓	↓	↓	↓	
Opaque corneal corpuscles in 2 days and slight edema	Cornea staining 1 day. Iritis	Early "moonstone eye." Severe iritis. Deposit on lens, 1 day	Discharge and extreme chemosis, 4 hr.	
↓	↓	↓	↓	
Silkiness 5–8 days. Disappears in a month or less	"Moonstone eye," 2 days	Invasion of cornea by vessels, 6 days	Chemosis better. Acute iritis 1 day	↓ Copious discharge, 5 days
	↓	↓	↓	↓
	Subsidence of edema, 6 days	Subsidence of edema and retrogression of vessels, 18 days	Invasion by vessels, 6 days	Hypopyon, 8 days
	↓	↓	↓	↓
	Recovery with fine silkiness, 16 days	Recovery with remains of vessels and depigmentation of iris, 3–4 weeks	Vessels reach central slough, 20–30 days	Perforation, 14 days
			↓	↓
			Separation of central slough or perforation, 20–34 days	Complete symblepharon and phthisis bulbi, 30 days
			↓	
			Phthisis bulbi and pigmentation of cornea, 2 months	

REFERENCES

[1] Mann, Ida, and Pullinger, B. D. A study of mustard gas lesions of the eyes of rabbits and men. Proc. Roy. Soc. Med., 1942, v. 35, No. 3, p. 229, Sec. 0, pp. 1-16. (Reprinted in Amer. Jour. Ophth., 1943, v. 26, p. 1253).

[1] —. Pathology of cholesterin and fat deposition in mustard-gas injuries of the cornea. Brit. Jour. Ophth., 1942, Nov., p. 503.

MACULAR EDEMA*

ARTHUR J. BEDELL, M.D.
Albany, New York

Edema of the macula may be an isolated condition or part of a general fundus change.

It is universally agreed that the macula varies in size from 1 to 3 mm. in diameter. In or near the center of it is the region of greatest differentiation and specialization. The absence of vessels in the macular region, the foveal depression, and the relatively thick surrounding retina must be considered as determining factors in the appearance of the lesions. Ophthalmoscopically, the macular region is often dark red, and almost invariably the surface changes can be recognized in stereoscopic examination or photographs.

For years, the bright spot seen with the ophthalmoscope in front of the fovea has been called the foveal reflex. It can be proved that the spot is very often absent in a healthy eye with normal, central visual acuity, and also that sometimes the reflex comes from different portions of the vitreous over the same macula in the photographs making a stereoscopic pair. Furthermore, this and the grosser macular reflexes are in front of the retina, vary greatly in visibility, are easily dispelled by a change in the angle of light reflection, and are on the vitreous. When the more delicate lesions, such as foveomacular disease, are studied, this understanding is essential to interpret correctly the faint changes and the exact placement of each. The macula, although commonly to the temporal side of the disc and slightly below the horizontal level, may be several millimeters above or below its usual location. This is one cause of head tilting and must be remembered in off-center macular edema. The macula may also be displaced laterally.

Some observers report that they have seen a hole at the macula develop after Berlin's edema. I have not been so fortunate, for, certainly in the usual case of the Berlin type, the edema is transitory and complete functional restoration the rule.

On several occasions I have photographed a circulatory macular destruction from the primary stage of a gray, localized edema, and slight reduction in central vision, through the various phases of infiltration and retinal absorption, until a clear, punched-out, red-based, permanent hole was formed. This type of hole is often smaller than the common, traumatic one, and, eventually, in a high percentage of cases, both eyes become involved.

The hole which results from detachment of the retina or intraocular inflammations may be sharply delimited, or the margins may be soft with an elevated surrounding ring. They may be shallow, suggesting a less complete destruction of the retina; a complete loss, which looks like a red opening in the gray retina; or the margins may form a ridge.

The casual observer may confuse a round mass of exudate in the macular region with either localized edema or a hole. Circumscribed hemorrhages may be incorrectly diagnosed as a hole. The absorption of the exudate, or the blood, will eventually prove the diagnosis. Occasionally, a perfectly round macular scar results from the partial destruction of the retina and choroid.

In sudden occlusion of the central vein,

* Presented at the 15th scientific meeting of the Association for Research in Ophthalmology, Inc., at San Francisco, July 2, 1946.

the retina is very edematous, and frequently an oval zone embracing the macula is especially prominent. In a branch closure, the edema extends from the closed vein over the macula. The blanched, milky-white edema of an abrupt closure of the central retinal artery is pathognomonic, and the macular red spot varies in size and color.

Stellate edema is characterized either by a circle of exudate spots about the edematous macula, or, and more often, by lines radiating from the macula toward the disc. As the edema subsides, the exudate spots decrease in number and, finally, if the case is observed long enough, they entirely disappear. The edema may be the result of an increased NPN without any other kidney dysfunction, or it may be part of a general hypertension.

In inflammations of the choroid or retina, the edema is often diffuse, covers a large macular surface, is thick, smoke-gray or yellow-tinged, and with or without hemorrhages. As the disease progresses, the edematous region decreases in size and thickness. In the terminal stage, a circumscribed white, plaquelike scar results, with or without pigmentation, and with or without vessels extending to and over it. There are many variations in the amount and disposition of the blood, its manner of absorption, its recurrence, and the association with cystic degeneration. Senile macular degeneration is frequently first observed as a circumscribed cloud of edema.

Another type of macular edema is that found in so-called retinitis circinata, which is not a disease but only a phase of a constantly changing fundus pattern of localized degenerations where a crown of exudate spots, thick, delicate, or even lacelike, surrounds the degenerating macula.

In 1928, I demonstrated photographs of what we then called preretinal edema. The term is just as appropriate now as then, for it accurately describes the location and appearance of the lesion.

When fluid collects over the macular retina, there is, in the early stages, a demarcating circle or oval of reflection on the pushed-forward vitreous, beneath which the fundus appears dark. The retinal vessels can be traced behind the reflex, and there is no "foveal reflex." As time passes, the reflecting circle enlarges with a corresponding increase in the darker area until, finally, the reflex disappears.

Gifford and Marquardt have called this angiospastic retinopathy but whether this, or central serous retinopathy, or any other term is used, the fundus edema is the same. The disease is said to be limited to young adults. I have seen it in middle and late life.

I have not seen macular drusen nor local holes develop after preretinal edema, which is usually unilateral, rapidly subsides, and leaves few, if any, pigmentary changes. The macular area may appear red, and probably that is the reason why it has been mistaken for a hole. The early vitreous reflex cannot be seen with an ordinary ophthalmoscope.

A Gullstrand or binocular ophthalmoscope or a Nordenson camera is essential, if the earliest signs of macular edema are to be recognized. Errors in diagnosis can be avoided by using red or green filters, reducing the illumination or using indirect illumination, as well as by shifting the light beam from side to side.

There is considerable risk in drawing conclusions regarding any particular therapy for this disease, which is often of short duration and, I believe, uninfluenced by any special treatment.

There are two other conditions which, at times, so closely resemble preretinal

edema that differentiation is impossible without stereoscopic studies or photographs. These are retinal edema and circumscribed retinal detachment.

Macular retinitis may be ushered in by true edema with a large vitreous reflex. This reflex may disappear, be absent some days or weeks, and then reappear, again to disappear as the exudate increases. In this edema, the fundus area is elevated, the retinal vessels are on the surface and can be traced only by stereoscopic examination. The dark-appearing base increases in diameter, as in preretinal edema, until it finally disappears, and the retina assumes its normal color or becomes scarred. The diagnosis of retinal edema depends upon the location of the retinal vessels on the surface of the convex dome of swelling.

Macular retinitis may, however, start with a very slight edema, not to be confused with either the preretinal or retinal edema with ring-shaped light reflexes. From a small, hazy, gray spot, the cloud increases and eventually terminates in a retinal scar. Another type forms a small circle with a pale center and close to it a spot of retinal depigmentation. In some cases, the edema extends from an adjacent, acute exudative retinitis over the macula.

There have been several articles on detachment of the retina at the macula. Idiopathic, flat detachment of the retina has been carefully presented in the thesis of Walsh and Sloan. In any case, where a detachment is suspected, it is necessary to exclude preretinal or retinal edema before reaching such a diagnosis. Here, again, stereoscopic photographs are of great value.

Detachment of the macular retina is very uncommon. Sometimes it is several disc diameters in size and so dark and so prominent that great care must be taken to differentiate it from a malignant growth of the choroid. Under such circumstances, repeated examinations are obligatory, and no eye should be sacrificed until the diagnosis is firmly established.

In some cases, the subretinal fluid is translucent, so that the outline of the detachment is readily seen. In others, as, for example, in myopia of high degree, a true cyst may partially or completely cover the macula. Some cysts are very small, while others may be more than a disc diameter in size and may be mistaken for a detachment.

The confusion in diagnosis is further increased if the patient is first examined when the condition is subsiding, for in all three—preretinal edema, retinal edema, and macular detachment of the retina—fine white specks, yellow dots, and minute or large pigmentations may develop and persist. These end results depend upon the duration, as well as the severity, of the local reaction, and it is difficult to anticipate or foretell with any degree of accuracy the exact terminal appearance of any given case.

During the past few months, several excellent articles on macular diseases have been published, and I wish to talk about some of them.

Adler and Scarlet, in their interesting paper, presented cases of juvenile macular choroiditis. Such cases are not rare. They are found in both males and females, start without demonstrable cause, follow a prescribed course, last many months, and although the fundus changes seem to vary little from week to week, they are, when carefully observed or photographed, continuous. There is a round, gray edema of the macular region, with some blood and a dark area near the center of the lesion, which, in the beginning, can only be seen with a red light. As time passes, the margin of the circle becomes more defined and the center so much

darker that it is readily seen with the light from any ophthalmoscope. The bleeding ceases, and eventually a circumscribed, round, gray-pigmented scar results. After the outer gray ring is once formed, it rarely increases in diameter. The end result may be a few, pale-gray or dense-black spots, a black ring, or a black center with a white, connective-tissue band across it. The circumscribed area, the uneven surface, the protracted course, and the recurring flat, granular hemorrhages are dominant characteristics of this type. Usually unilateral and occurring in young adults, I have, however, seen it in both eyes in late life.

The critical analysis of central visual impairment reported by Cordes for the group of Navy ophthalmologists is not only comprehensive and well done, but also thought-producing, for it stimulates all ophthalmologists to be accurate in the recognition of small deviations from the normal and correct in their interpretations.

Some months ago, before the Cordes report, I talked with him and said that I had been seeing peculiar macular lesions in young adults in the Army, as well as some officers in the Navy who had been in the earliest South-Pacific campaign. It is unfortunate that photographic records were not kept for patients in the European theater.

In the Cordes report, it is noted that, in certain types of trauma, there is a partial destruction of the macular region. The outline of the reddish area is indefinite, as it fades into the surrounding, normal-appearing retina, and looks like an incomplete hole. On closer inspection, the lesion is found to be a puckered scar, the apex of which is white and elevated, suggesting an accentuated, so-called foveal reflex.

In other cases, the macula is red and slightly depressed, showing a genuine, superficial, partial destruction of the retina.

The study of complicated fundus patterns frequently leads to the correct interpretation of local changes. In a case of traumatic macular retinochoroiditis with retinitis proliferans, delicate hemorrhages were seen in the proliferans, as well as a pink spot which looked like a small hole in the retina. This was easily proved to be an opening in the proliferating sheet through which the red fundus background was visible. It is not improbable that some reported cases of hole at the macula may come under this group.

As an example, the same suggestion of a macular hole was found in the left eye of a young soldier whose fundus I had photographed and found normal before he entered the Service. He had recently noted a marked reduction in vision. To the outer side of the macular region was an elevated, gray layer with an almost circular, pink center, which was the retina seen through the overlying vitreous edema. When the acute stage subsided and the gray edema of the vitreous had disappeared, there were several pigmented granules over what had been the pink spot.

Most of the Service-connected cases, as well as those in civilian life, have been unilateral. The etiology is unknown.

Summary

The common causes of edema of the macular region have been demonstrated.

Special attention has been drawn to Berlin's edema, the various causes for holes at the macula, and the inflammatory reactions of retinochoroiditis and retinitis.

In hemorrhagic exudate or traumatic hole, it is very probable that there is always some edema at some time, and, for that reason, examples of each are included.

Preretinal and retinal edema have been explained as a pushing outward of the vitreous, producing the ring-shaped light reflex which is on it.

Some of the recent papers on macular edema have been referred to, and additional illustrations of juvenile macular degeneration, central serous retinopathy, local detachment of the retina, and foveo-macular diseases have been presented.

Conclusions

An edema of the macular region may be the isolated expression of a local or general tissue reaction. The edema may be limited to and disappear from the macula, or it may be the precursor of an extensive retinochoroiditis or gross macular change. The healed macula may show pigmented specks, white dots, heaped-up pigment, atrophy, or thick scars which may be smooth and flat, or rough and nodular.

This essay was illustrated by a series of Kodachrome photographs.

344 State Street.

Bibliography

Adler and Scarlet. Juvenile macular exudative choroiditis. Arch. of Ophth., 1944, v. 31, p. 144.

Batten. Classification of the macular diseases. Trans. Ophth. Soc. United Kingdom, 1921, v. 41, p. 411.

Bailliart. L'oedeme de la retine. Annals d'Ocul., 1938, v. 175, p. 133.

Bedell. A photographic study of holes in the macular region and some other associated changes. Amer. Jour. Ophth., 1927, v. 10, Dec., p. 890; Trans. Amer. Ophth. Soc., 1927, v. 25, p. 143.

———. An exposition of some round macular lesions. Trans. Amer. Ophth. Soc., 1939, v. 37, p. 185.

———. Traumatic changes in the retina, choroid, nervehead, and vitreous. Jour. Amer. Med. Assoc., 1941, v. 117, p. 1774.

———. Clinical ophthalmoscopy. Albany, New York, J. A. Glenn, 1946.

Clapp. Hole at the macula. Ophthalmic record, 1913, v. 22, p. 79.

Collins. Subchoroidal hemorrhage from concussion and its relation to (a) commotio retinae; (b) holes at the macula; (c) pigmentation of the retina; (d) pigmentary disturbance at the macula. Trans. Ophth. Soc. United Kingdom, 1917, v. 37, p. 112.

Cordes. A type of foveo-macular retinitis observed in the U. S. Navy. Amer. Jour. Ophth., 1944, v. 27, p. 803.

Dimmer and Pillat. Atlas photographischer Bilder des menschlichen Augenhintergrundes. Franz Deuticke, 1927. Tafel 39.

Duke-Elder. Text book of ophthalmology. St. Louis, C. V. Mosby Co., 1941, v. 3, pp. 2588, 2592, 2595.

Fuchs, E. Zur Veränderung der Macula lutea nach Contusion. Zeit. f. Augenh., 1901, v. 6, p. 181.

———. Lochbildung in der Fovea centralis. Graefes Arch., 1911, v. 79, p. 42.

———. Ein Fall zentraler rezidivierender syphilitischer Netzhautentzündung. Central. f. Prak. Augenh., 1916, v. 40, p. 105.

———. Ueber Beteiligung der Macula lutea an Erkrankungen des Auges. Graefes Arch., 1918, v. 97, p. 57.

Gifford. Evaluation of angiospasm. Arch. of Ophth., 1944, v. 31, p. 453.

Gifford and Marquardt. Central angiospastic retinopathy. Arch. of Ophth., 1939, v. 21, p. 211.

Gissy. Ein weiterer Fall von praeretinalem Oedem. Zeit. f. Augenh., 1925, v. 57, p. 423.

Greeves. Macular edema. Trans. Ophth. Soc. United Kingdom, 1941, v. 61, p. 5.

Guist. Ueber praeretinales Oedem. Zeit. f. Augen., 1925, v. 54, p. 37.

Kitahara. Ueber klinische Beobachtungen bei der in Japan häufig vorkommenden Chorioretinitis centralis serosa. Klin. M. f. Augenh., 1936, v. 97, p. 345.

Lijo Pavia. Fondo de ojo. Edema macular, etc. Rev. Oto-Neuro. Oftal., 1935, v. 10, Nov., pp. 303-309.

Lowenstein. Retinopathia centralis angiospastica (angioneuritica) and serosa allergica and their relation to detachment of the retina. Brit. Jour. Ophth., 1941, v. 25, p. 369.

Loring. Hole around the macula lutea. Trans. Amer. Ophth. Soc., 1871, p. 72.
MacRae. Bilateral macular disease. Trans. Ophth. Soc. United Kingdom, 1934, v. 54, p. 530.
Nano. Chorio-retino central seroso. Semana Méd., 1941, v. 2, July 3, p. 37.
Parsons. Partial thrombosis of the central vein. Trans. Ophth. Soc. United Kingdom, 1907, v. 27, p. 121.
Philips. Traumatic oedema of the macula. Brit. Jour. Ophth., 1943, v. 27, p. 305.
Pittar. A case of hole at the macula due to looking at the sun. Brit. Jour. Ophth., 1943, v. 27, p. 36.
Plummer. Retinal allergy. Arch. of Ophth., 1937, v. 74, p. 516.
Samuels. Cystic degeneration of the retina. Arch. of Ophth., 1930, v. 61, p. 476.
deSchweinitz. Concerning certain non-traumatic perforations of the macula lutea. Trans. Amer. Ophth. Soc., 1904, v. 10, p. 228.
Smith. Actinic macular retinal pigment degeneration. U. S. Naval Med. Bull., 1944, v. 42, p. 675.
Walsh and Sloan. Idiopathic flat detachment of the macula. Amer. Jour. Ophth., 1936, v. 19, p. 1935.
Williamson. Two cases of thrombosis of the retinal vein; one showing a hole, the other a star at the macula. Brit. Jour. Ophth., 1922, v. 6, p. 67.
——, and Noble. Open holes in the retina. Trans. Ophth. Soc. United Kingdom, 1941, v. 61, p. 192.
Wolf. Macular degeneration in iridocyclitis. Proc. Roy. Soc. Med., 1931, v. 24, p. 1617.
——. The anatomy of the eye and orbit. Philadelphia, Blakiston Co., 1940, p. 90.
Zeeman. Retinitis centralis angioneurotica (Horniker). Klin. M. f. Augenh., 1931, v. 87, p. 548.
Zentmayer. Hole at the macula. Ophth. Record, 1909, v. 18, p. 198.

Discussion

Dr. Ralph I. Lloyd (Brooklyn): Will you give an idea of the apparatus used in making the diagnosis of this group of fundus lesions?

Dr. Bedell (closing): The diagnosis of all fundus lesions is made by the use of the ordinary ophthalmoscope with red, green, and yellow filters and the Nordenson camera. The finest diagnostic detail is seen with the Nordenson and confirmed by the study of stereoscopic Kodachrome photographs.

THE RELATION BETWEEN MATERNAL VITAMIN-A INTAKE, BLOOD LEVEL, AND OCULAR ABNORMALITIES IN THE OFFSPRING OF THE RAT*

BLANCHE JACKSON, PH.D., AND V. EVERETT KINSEY, PH.D.
Boston, Massachusetts

The experimental production of congenital eye lesions by means of maternal vitamin-A deficiency has been demonstarted in several animal species. The literature on this subject has been reviewed recently by Warkany.[1]

In the rat, the eyes of offspring born by vitamin-A-deficient mothers may show abnormalities resembling in some respects the condition of retrolental fibroplasia as found in man. The following eye defects are some of those described by Warkany and Schraffenberger as appearing in the rat: absence of anterior chamber, iris, and ciliary body; failure of vitreous formation, with the development in its place of connective tissue; eversion of the retina, and retinal disorganization.[2, 3] These workers observed considerable variation in the degree of abnormality occurring in different litters. In some instances, the defect consisted only in the development of a retrolenticular mass of connective tissue.

The object of the present investigation was to attempt to repeat Warkany and Schraffenberger's findings and at the same time to determine the degree of the deficiency in the mothers which will lead to ocular maldevelopment.

EXPERIMENTAL PROCEDURE

Albino rats of the Sprague-Dawley strain were used. The Warkany procedure was followed in the first three experiments by placing female weanlings on a basal vitamin-A-deficient preparatory diet (Warkany's diet U[1])† supplemented with vitamin D and with carotene sufficient to allow growth and sexual maturation, but insufficient to allow the accumulation of significant hepatic stores. To mate the rats during the working day, their diurnal rhythms were reversed; this was accomplished by keeping them in rooms with reversed periods of light and dark. During this preparatory period, the animals were housed in large cages provided with wire-mesh floors; about 10 rats were kept in each cage. When the females were 90 to 100 days old, they were transferred to individual cages and fed a purified diet deficient in vitamin A (Warkany's diet W[2]).‡ Following Warkany, each animal received an oral dose of 50 I.U. of vitamin D, 2.5 mg. of α-tocopherol, and 10 micrograms of 2-methyl naphthoquinone every 10 days. Crystalline carotene (Smaco) dissolved in Wesson oil, or vitamin A, was administered orally as indicated in the separate experiments. For the mating of these females, healthy male rats of the same strain were used. In most instances, the time of mating was determined within a few hours by the presence of a vaginal plug or sperm.

Blood samples used for vitamin-A determination were obtained from the tail

* From the Pathology Laboratories of the Massachusetts Eye and Ear Infirmary and the Harvard Medical School. Presented at the 15th scientific meeting of the Association for Research in Ophthalmology, Inc., in San Francisco, July 2, 1946.

† Percentage composition of Warkany and Schraffenberger's preparatory diet: Ground whole wheat, 74; crude casein (Borden), 15; brewers' yeast (Mead Johnson), 10; sodium chloride, 1.

‡ Percentage composition of Warkany and Schraffenberger's purified diet: Sucrose, 68; vitamin-test casein, 18; vegetable oil, 10; salt mixture, 4.

vein at least 20 hours after the administration of any vitamin-A supplement. When a sample was taken just prior to killing the animal, it was obtained by cardiac puncture. Vitamin-A analyses were made on approximately 0.1 ml. blood serum, according to the micro-method developed by Lowry and Bessey.[4]

First experiment. The first experiment was designed simply to reproduce Warkany's experiments. Fifty-seven female rats 25 days old were placed on the preparatory diet. They received 25 micrograms of carotene on the 34th, 44th, and 54th days of age. Because the animals showed more rapid growth than Warkany's,* the carotene supplement was then discontinued. On the 89th day, animals showing marked signs of vitamin-A deficiency were placed on the purified diet supplemented with one or two doses of 25 micrograms of carotene. On the 93d day, the remaining animals were transferred to the purified diet, and mating was begun. At this stage, many of these animals showed severe signs of vitamin-A depletion. The fur was dirty and stained, there were deposits of reddish material (porphyrin?) about the eyes, and the eyes showed the xerophthalmia characteristic of vitamin-A deficiency. Some animals exhibited respiratory difficulty. Nine rats died at 91 to 110 days of age, before being mated; at autopsy several were found to have kidney disorders involving infection, enlargement, and/or stone formation. To prevent more deaths, a maintenance dose of vitamin A (20 I.U. orally about every 10 days) was given to the remaining rats during the period of mating and gestation.

Thirty animals were mated shortly after the diet change, and of these, 20 became pregnant. Five of the pregnant animals died within three weeks after mating. At the time of death, two of these had completely resorbed their fetuses; three had fetuses 18 to 19 days old which could be used for histologic examination. Six pregnant animals were killed 14 to 24 days after mating; five had fetuses in various states of resorption; one, however, had eight live 21-day old fetuses which could be used for histologic study. The other nine pregnant rats resorbed their litters. Thus, from 57 animals, fetuses in an advanced state of development were obtained from but four mothers.

Terminal vitamin-A analyses were made on two of the four animals which carried their young nearly to term. In both instances, the serum vitamin A was less than 5 I.U. per 100 ml. (the normal blood serum vitamin A for mature female rats of this strain is about 75 I.U. per 100 ml.) Further evidence that this is a vitamin-A deficiency is seen in the weight response of the animals to small doses of vitamin A (fig. 1).

The eyes of the young in all four litters exhibited ocular abnormalities essentially similar to those described by Warkany. Complete serial sections of the two eyes of one fetus from each litter were made, in addition to nonserial sections on two or three other members of each litter. In every instance, there was a retrolental mass of connective tissue; in the eyes from three litters it extended from the lens to the region of the nerve head. In all except one animal, there was marked retinal folding. In several eyes, there was slight retinal eversion near the nerve head. In one specimen (18-day), the fetal fissure had failed to close at any point. Large hemorrhages in both the primary

* This apparent discrepancy in growth rates was clarified by correspondence with Dr. Warkany. The original value cited in his first paper was a numerical error, since 4 micrograms instead of 25 micrograms of carotene were given every 10 days.

optic vesicle and the vitreous space were found in the eyes from two of the litters. Sections made from one of the abnormal eyes are shown in plate I. These abnormalities appear to be somewhat less severe than those studied by Warkany. For example, there were no cases of young carried to term with the "open eyes" which Warkany and Schraffenberger described.

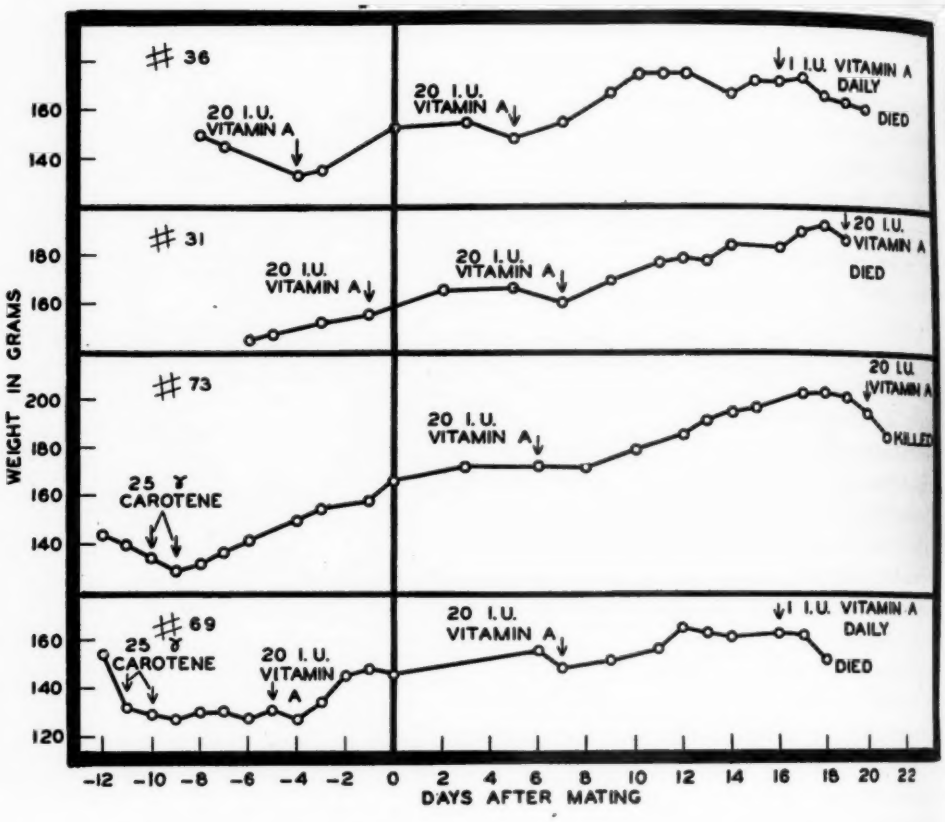


Fig. 1 (Jackson and Kinsey). Weight curve of four rats producing litters with abnormal eyes. Note growth response to additions of carotene or vitamin A.

Second experiment. The object of the second experiment was to determine the maximal daily dose of vitamin A which, when given to females depleted of their vitamin stores, would result in development of eye abnormalities in the offspring. The animals used were a group of the original lot employed in the first experiment—those which were still unmated after several weeks on the purified diet and those which had resorbed their first litters. The animals were separated into groups and given daily doses of 2, 3, 5, or 10 I.U. of vitamin A daily.

The general condition of the animals in this experiment was superior to that in experiment 1. Moreover, they showed a more uniform physical state through the experimental period, presumably because they received vitamin A daily, rather than at 10-day intervals. Marked symptoms of ill-being were noted only at the end of pregnancy and seemed to be related to

difficult parturition or inability to deliver.

From the mothers receiving 2 I.U. of vitamin A daily, only one mature fetus was obtained. This fetus had normal eyes. The serum vitamin-A level in the mother on the 22d day of pregnancy was 24 I.U. per 100 ml.

Three litters were obtained from mothers receiving 3 I.U. daily. Of six fetuses in one litter, three had ocular abnormalities, including an orbital cyst (one case), retinal folding, and retrolental connective tissue. In the second litter, of four fetuses sectioned but one showed any abnormality, and this consisted only of retinal folding. Three of the eight young in the third litter were sectioned, and all three were found to be normal. The abnormalities consisted of retinal folding and retrolental masses of connective tissue, as may be seen from plate II. Serum vitamin-A levels of the three mothers in this group, taken at various times during pregnancy, ranged from 0 to 12 I.U. per 100 ml.

The eyes of four litters carried to term by mothers receiving 5 I.U. of vitamin A per day were studied histologically. One of two fetuses sectioned from one litter showed abnormal retinal folding in the upper portion of one eye and a coloboma. One specimen from another litter also exhibited retinal folding and slight eversion of the retina. The four members of the other two litters studied had normal eyes. Serum vitamin-A values for these mothers on the 21st to 22d day of pregnancy ranged from 6 to 21 I.U. per 100 ml.

Three mothers receiving 10 I.U. per day produced young with normal eyes. Serum samples collected from the mothers 9 to 22 days after mating gave a range of 12 to 54 I.U. of vitamin A per 100 ml., the average being 35 I.U.

The results of this experiment indicate that ocular abnormalities are obtained from rats previously depleted of vitamin-A stores only when the dose of vitamin A does not exceed 3 to 5 I.U. per rat per day. Furthermore, the degree of abnormality appears to be related inversely to the daily intake, so that at the 5-I.U. level,

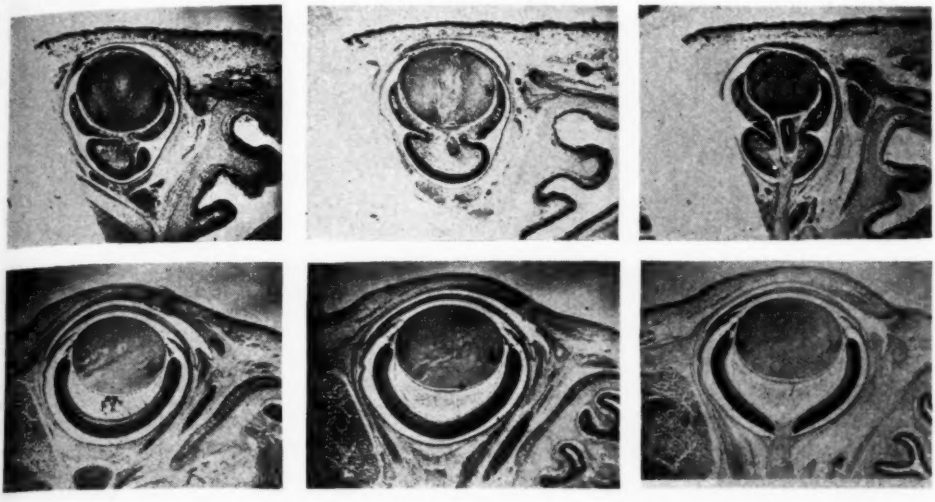


Plate I (Jackson and Kinsey). A, B, and C are transverse sections taken approximately one third, one half, and two thirds from the top of the eye, respectively, of an abnormal fetus about 19 days old. Sections D, E, and F are from a normal 19-day rat fetus.

except for one case of coloboma, only abnormal retinal folding was observed.

Third experiment. In the previous experiments, the yield of mature live young with severe ocular malformations was very low. In addition to the high percentage of resorptions, many young died before the weanling stage were placed on the preparatory diet and given 12.5 micrograms of carotene every 10 days. The final dose before the change to the purified diet was double this amount. At the time the animals were put on the purified diet, daily supplements of 1 or 2 I.U. of vitamin A were begun. Control animals

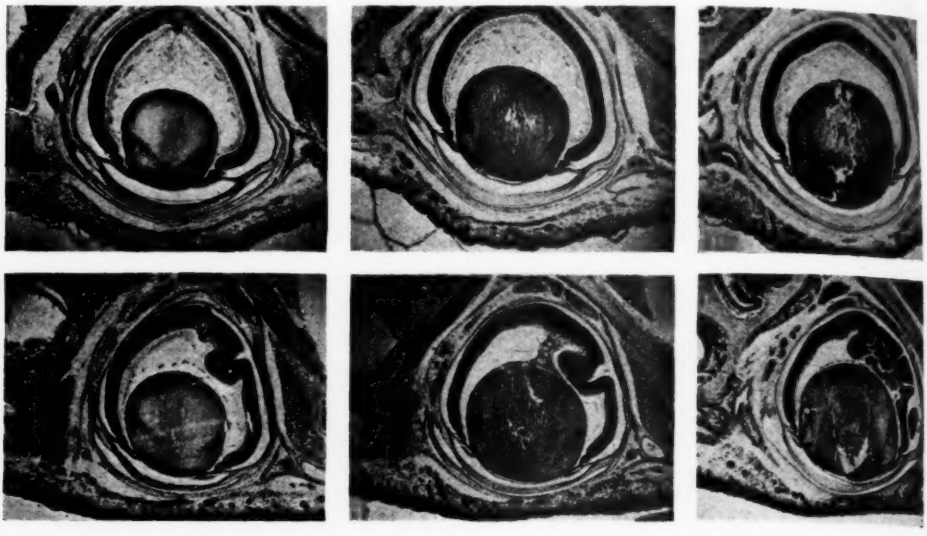


Plate II (Jackson and Kinsey). A, B, and C are transverse sections through an abnormal eye of a mature (22-day) rat fetus. Sections D, E, and F are from a control rat killed at birth (22-day gestation period).

cause the mothers were too depleted to deliver them. Since Warkany and Schraffenberger had observed the eye defects as early as the 15th day of fetal life, it was thought that the abnormal young might be carried to term and delivered by the mothers maintained on low vitamin A until the 15th day and then given adequate amounts of the vitamin. A second approach to the problem was suggested by Mason's finding that the resorptions occurring in vitamin-A deficient rats are indirectly associated with bacterial infection.[5] In an attempt to offset this occurrence, the mothers were treated with sulfathiazole and with penicillin.

Two groups of rats were used for these experiments. In the first, 36 animals in (five) were given 100 I.U. daily. On the 15th day after mating, the daily supplement to the low vitamin-A group was increased to 100 I.U.

Only one mature fetus was obtained for histologic examination, and this was taken by Caesarian section. It did show, however, the characteristic eye abnormalities. Analyses of the mother's serum vitamin A on the 0, 5, 10, and 15th days of pregnancy gave values of 12, 11, 5, and 10 I.U. per 100 ml., respectively. Somewhat higher values were obtained on other animals which resorbed their litters completely and at an earlier stage of gestation. Control animals delivered normal, live young.

The second group of animals received

12.5 micrograms of carotene throughout the preparatory period. They, too, received daily vitamin-A supplements of 1 or 2 I.U. after being changed to the purified diet. Some of the animals received sulfathiazole at a 1-percent level in the food for the first 15 days after mating. Others were injected with penicillin (500 Ox. u. in 0.1 ml. of vegetable oil) twice daily on the 8th through the 12th day after mating. On the 15th day of pregnancy, the mothers were changed from the purified diet to a commercial stock ration.

No full-term fetuses were obtained from the mothers kept on low levels of vitamin A during the first two weeks of pregnancy. Analyses of 19 blood samples collected during the first 15 days of pregnancy from seven mothers which resorbed their litters showed the average serum vitamin A to be 6 I.U. per 100 ml. (range 0 to 20). The average of 12 determinations on similar samples from five control animals was 51 I.U. (range 28 to 81).

Fourth experiment. In still another attempt to obtain live young showing eye abnormalities, female rats were allowed to grow normally to maturity on a complete stock ration and then depleted of their vitamin-A stores to varying degrees. The animals were put on the Warkany purified diet at 110 days of age. After periods of 5 to 13 weeks, they were mated. To keep the blood-vitamin-A level at a relatively constant value during the early period of pregnancy, some of the animals were given 1 or 2 I.U. daily. As in the previous experiments, additional vitamin A was supplied on the 15th day after mating. In the present experiments, this was accomplished by placing the animals on the commercial stock ration.

Complete data on this group are given in table 1. It will be observed that, from the 135 live young born, none showed the eye abnormalities described by Warkany and Schraffenberger, although in two instances some retinal folding was observed (Nos. 169 and 190). The occurrence of this condition was probably related to the fact that the mothers of these two litters were severely depleted of vitamin A. In general, only essentially normal young were carried to term; mothers very low in vitamin A resorbed their litters. If the number of mothers depleted to such low levels associated with fetal resorptions had been greater, it is possible that a small percentage of abnormal litters might have been obtained.

Discussion

Results cited previously have indicated that the ocular abnormalities occur only with daily vitamin-A allowances of less than 3 to 5 I.U. It is important to correlate the ocular defects with the various serum levels of vitamin A which were taken from time to time throughout the period of pregnancy. In all the animals producing young with abnormal eyes, the serum vitamin-A levels were less than 12 I.U. per 100 ml.; normal eyes were obtained when the maternal-serum vitamin-A level was only slightly greater than this. Thus, ocular defects occur in the young of rats having serum levels approximately one tenth or less of the normal.

It is worth noting that no vitamin-A deficient mothers seemed to be able to deliver their abnormal young. Although some defective fetuses may be carried to term, the amount of vitamin A required for successful parturition seems to be beyond the range of that associated with the production of ocular abnormalities.

Warkany and Schraffenberger reported that the vitreous was lacking in the abnormal eyes, the space which it would normally occupy being filled with the retrolental connective tissue. Although we

TABLE 1

DATA ON NUTRITIONAL EXPERIMENTS ON 19 FEMALE RATS

No.	Days on Deficient Diet at Mating	Daily Vit.-A Supplement. Days 0–15 of Pregnancy	Serum Vit. A—I.U.% Days after Mating					Notes on Pregnancy	Eyes of Offspring
			0	5	10	15*	20		
173	35	0	60	—	59	43	29	Delivered 9 dead young on 22d day.	Normal (histol. examination.
179	46	0	63	53	40	9	16	Delivered 10 live young on 23d day, 5 left with mother; 2 of these eaten, 3 weaned.	Normal (histol. exam. and exam. with ophthalmoscope of weanlings).
177	52	0	41	56	34	26	32	7 live young taken by Caesarian 24 days after mating.	Normal (histol. examination).
183	52	0	32	30	12	14	45	Delivered 7 live young on 23d day.	Normal (histol. exam. and exam. of weanlings with ophthalmoscope).
192	52	0	8	16	18	12	38	Delivered 7 live, 1 dead young on 23d day. Young left with mother were eaten.	Normal (histol. examination).
164	39	1 I.U.	61	61	—	—	41	Delivered 11 live young, late 22d day.	Normal (weanlings examined with ophthalmoscope).
161	41	1 I.U.	83	—	—	24	55	Delivered 8 live, 2 dead young, late 22d day.	Normal (weanlings examined with ophthalmoscope).
186	41	1 I.U.	—	—	32	21	52	Delivered 10 live young, late 22d day.	Normal (histol. exam. and exam. of weanlings with ophthalmoscope).
180	76	1 I.U.	6	—	8	18	—	Killed 15th day because of resorbing. 2 live, 1 dead fetuses.	No abnormality could be recognized at this stage.
182	40	2 I.U.	57	—	29	—	48	Delivered 6 live young, late 23d day. 2 of 5 left with mother died.	Normal (histol. exam. and exam. of weanlings with ophthalmoscope).
172	41	2 I.U.	66	47	—	41	62	Delivered 7 live young, late 22d day.	Normal (histol. exam. and exam. of weanlings with ophthalmoscope).
181	42	2 I.U	53	—	26	16	55	Delivered 5 live young late 22d day	Normal (exam of weanlings with ophthalmoscope)
190	94	{1 I.U., days 0–15 3 I.U., days 6–15}	10	8	4	28	71†	Delivered 2 live, 4 dead young, 23d day. The 2 live young left with mother were killed.	Slight retinal folding (histol. examination).
178	77	{2 I.U., days 0– 6 0 I.U., days 7–14}	19	16	—	—	—	Killed 14th day because resorbing. 14 resorption sites.	
184	80	{1 I.U., days 0– 9 2 I.U., days 10–14}	14	6	0	8	—	Killed 15th day because resorbing. 11 live, 2 dead fetuses.	No abnormalities could be distinguished at this stage.
169	41	0 (throughout entire pregnancy.)	—	—	—	9	14‡	Delivered 5 live, 3 dead young. Mother killed 3 live young left with her.	Retinal folding.
163	40	100 I.U.	63	65	—	—	40	Delivered 4 live, 6 dead on 23d day. 2 live left with mother were eaten.	Normal at weaning.
176	41	100 I.U.	41	—	41	45	71	Delivered 11 live young, 22d day.	Normal (histol. exam. and exam. of weanlings with ophthalmoscope).
189	42	100 I.U.	81	—	45	43	59	Delivered 10 live young, 22d day.	Normal at weaning.

* Put on Rockland rat pellets on 15th day of pregnancy.

† In addition to being changed to commercial rat pellets on 15th day. No. 190 received 100 I.U. vitamin A per day on days 15–23.

‡ No. 169 was maintained on the purified diet without any vitamin-A supplement throughout pregnancy.

also observed eyes where this occurred, in some instances the retrolental mass was considerably reduced and vitreous was present. This would appear to represent

one of the variations in degree of the effects produced by the vitamin-A deficiency.

Marked folding of the retina (or inner layer of the optic cup) is one of the most striking features observed in the abnormal eyes. In some cases, it reduces considerably the space which in normal eyes is occupied by the vitreous body. In many eyes, the folding seems to be definitely the result of overgrowth of this layer, a condition which could lead to the retinal eversion frequently observed. Retinal folding, especially in the upper part of the eye, seems to be the first abnormality encountered as one goes from completely normal eyes to those of increasing degrees of malformation.

Summary and Conclusions

Following techniques devised by Warkany and Schraffenberger, a group of 57 weanling female rats were grown to maturity without the accumulation of hepatic stores of vitamin A. They were then bred and given only minimal amounts of vitamin A during pregnancy. Four of the mothers carried their fetuses to advanced stages of development. The eyes of the young in these litters showed the abnormalities which have been described by Warkany and Schraffenberger.

To determine the limiting level of vitamin-A dosage in female rats producing young with abnormal eyes, similarly prepared female rats were given 2, 3, 5, or 10 I.U. of vitamin A daily. They were then bred, and the supplement was continued at the same level. Young obtained from mothers fed less than 3 to 5 I.U. daily showed the eye defects already mentioned, whereas those receiving more than this amount of the vitamin all had normal eyes, even though the vitamin-A dosage was insufficient to allow normal delivery in many cases.

Serum vitamin-A values, taken during pregnancy from female rats producing young having abnormal eyes, were found to be less than 12 I.U. per 100 ml. in every instance (normal, 75 I.U. per 100 ml.). The addition of 100 I.U. of vitamin A daily or the feeding of a stock ration after the 15th day of pregnancy, with or without treatment with penicillin or sulfathiazole, did not reduce the high percentage of fetal resorption observed in the previous experiments.

It is concluded that ocular defects occur in the young rat only when the maternal vitamin-A deficiency is extremely severe, so advanced, in fact, that fetal resorption is common and normal birth is impossible.

To the extent that the physiologic processes associated with reproduction in human beings parallel those in the rat, it may be inferred that vitamin-A deficiency in the mother is not a probable cause of retrolental fibroplasia.

243 Charles Street (14).

References

[1] Warkany, J. Manifestations of prenatal nutritional deficiency. Vitamins and Hormones, 1945, v. 3, p. 73.

[2] Warkany, J., and Schraffenberger, E. Congenital malformations of eyes induced in rats by maternal vitamin A deficiency. Proc. Soc. Exp. Biol. Med., 1944, v. 57, p. 49.

[3] Warkany, J., and Schraffenberger, E. Congenital malformations induced in rats by maternal vitamin A deficiency: I. Defects of the eye. Arch. of Ophth., 1946, v. 35, p. 150.

[4] Lowry, O. H., and Bessey, O. A. Microchemical methods for nutritional studies. Federation Proc., 1945, v. 4, p. 268.

[5] Mason, K. E. Foetal death, prolonged gestation, and difficult parturition in the rat as a result of Vitamin A deficiency. Amer. Jour. Anat., 1935, v. 57, p. 303.

Discussion

Dr. Conrad Berens, chairman (New York): This is a piece of research which is so vital in the prevention of blindness. We know that about 51 percent of blindness in the schools for the blind is caused by congenital abnormalities.

Dr. Derrick Vail (Chicago): Were there any skeletal malformations, especially in the optic foramen, base of skull, and so forth, observed?

Dr. V. Everett Kinsey (Boston): We have not yet examined the eyes or the animals for other defects including skeletal abnormalities, so I am unable to answer that question. Warkany, I believe, has described such defects in detail.

Dr. Vail: I should like to say just a few words, if I may. I want to inject here a note of warning. A few weeks ago, I testified in a criminal court case brought against a quack vitamin specialist who cited experimental work, reported in Iowa, on vitamin-D deficiency as a cause of anophthalmos in a litter of new-born pigs.

In his pamphlets, broadcast widespread to the public, he used the reports of these experiments to terrify pregnant women and urged them to buy his vitamin product as a prevention of blindness in the unborn child.

I should like to have, some place in the discussion, a firm statement to the effect that the results of your experiments are not yet applicable to human beings.

Dr. Kinsey: I think our conclusion was to the effect that, in so far as the physiologic processes were the same in rats and in human beings, vitamin-A deficiency is not a probable cause of retrolental fibroplasia.

Even though we have to change our minds, I think, for the record, it might be well to be over cautious and say definitely that these results do not suggest that maternal vitamin-A deficiency is in any way associated with ocular abnormalities in infants.

Dr. T. L. Terry (Boston): It is not intended to detract from this presentation, but I think it would interest you to know that pediatricians working on the problem of retrolental fibroplasia found clinically that this abnormality, which Jackson and Kinsey have reproduced, has developed in two infants whose vitamin-A blood level was kept normal by therapeutic measures. It may interest you further that, according to Clifford and Allers, vitamin A, when dissolved in oil, is not absorbed by the premature infant from the gastrointestinal tract, nor is it absorbed following subcutaneous or intramuscular injection. If the vitamin A is dissolved in glycerol instead of oil, they found that the level of the vitamin in the blood is elevated. In two infants who had received such injections, retrolental fibroplasia developed despite normal vitamin-A levels in the blood.

INTRAOCULAR MANIFESTATIONS OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS*

REPORT OF A CASE

FERDINAND L. P. KOCH, M.D.
New York
AND
(BY INVITATION)
WILLIAM P. MCGUIRE, M.D.
Winchester, Virginia

The paucity of adequate descriptions of the eyegrounds in instances of acute disseminated lupus erythematosus, with the exception of Maumenee's contribution, appears to be rivaled only by the infrequency with which such pertinent observations accompany reports of this disease in the medical literature. It is hopefully anticipated that an entity exhibiting such protean manifestations of a vasculo-allergic character be the subject of the integrated attention of the ophthalmologist, the internist, and of the dermatologist, each of whom, within his special field, encounters deviations from the normal. Many of these are exemplified in the following condensed case report.

B. L., an unmarried Jewess, aged 22 years, and of asthenic habitus, was admitted to the Presbyterian Hospital in October, 1938, with a history of recurrent fever and malaise for the preceding six weeks. She had had, however, frequent, migratory, multiple joint pains, chronic pharyngitis, cervical adenopathy, leucorrhea, and intermittent fever during the two years since October, 1936, in which month the differing diagnoses of septic sore throat and scarlatina had been made by local physicians. Infectious arthritis also had been considered. There had been one bout of severe erythema of diffuse distribution of four to five days' duration six months prior to the patient's admission. The rash and temperature had subsided simultaneously. Exacerbations, however, tended to recur with the advent of cold weather and were accompanied by weakness and anorexia. General examinations, as well as symptomatic treatment by numerous local physicians, consistently yielded essentially negative results. Her past history was otherwise irrelevant.

A questionable systolic murmur at the apex, normal blood pressure, enlargement of a small tender lymph node in the right axilla, a thick malodorous leucorrhea, and a virginal introitus were the only positive findings on general physical examination at the time of admission to the Hospital. All of the indicated special examinations were made: X-rays of the chest, abdomen, viscera, and skeleton were negative; agglutination tests for hemolytic streptococcus (group A), typhoid, typhus, paratyphoid, and brucellosis were negative as was the Frei test; specific allergy testing was not undertaken, but intracutaneous testing for brucellosis and tuberculosis yielded

*From the Departments of Ophthalmology, Bellevue Hospital and New York University. Manhattan Eye, Ear and Throat Hospital. Presented at the eighty-first annual meeting of the American Ophthalmological Society at Hot Springs, Virginia, November, 1945.

Appreciation is expressed for the courtesy extended by the Department of Medicine, College of Physicians and Surgeons, Columbia University, for permission to present observations by the staff and the authors during their association with the Institute of Ophthalmology of the Presbyterian Hospital.

negative results. There was mild hypochromic anemia with moderate leucopenia (relative) and slight hemoglobinemia; no parasites were found in the blood or stool, and blood cultures were negative; serum protein was very slightly reduced, and there was a moderate hyperglobulinemia. The results of blood-chemistry tests were otherwise normal. Sedimentation rate was 54 mm. in the first hour; urinalysis revealed slight albuminuria; and biopsy examination of the enlarged right axillary node revealed a mild nonspecific lymphadenitis, with no bacterial growth on culture.

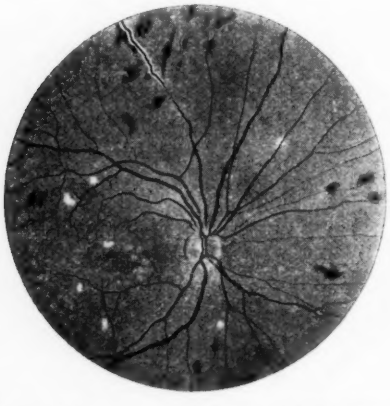


Fig. 1 (Koch and McGuire). O.D. drawing, February, 1939.

The course under hospital and convalescent home care, until the patient's death on September 25, 1939, was essentially one of remissions and exacerbations of muscular and joint discomfort, elevation of the temperature to an occasional high level of 104°F., but of no characteristic type, upper respiratory infections and bronchopneumonia, maculopapular erythema of irregularly diffuse distribution, maintenance of normal diastolic and systolic blood pressures, abdominal pain with tenderness and spasm, mental irritation, and increasing apprehension as discomfort and diminishing vision progressed.

By gradual exclusion the clinical diagnosis of acute disseminated lupus erythematosus was decided upon approximately three months after the patient was admitted to the hospital. Laboratory findings, on frequent examinations, were somewhat variable, but the general trend during her illness continued to be one of increasing deviations from the normal in the directions indicated on the first tests performed after admission. The exception to this was the continued variability of the Kline and Wassermann reactions no matter what antigen was employed. Treatment included all suggested symptomatic aids, physiotherapy, sulfonamides, and the customary antisyphilitic agents, any one or all of which may have been without effect or may have initiated remissions or exacerbations. Autopsy permission was refused by the male parent.

Ophthalmoscopically, no observations were made except by the medical house officer (who reported the fundi normal on admission) until a complaint was made of blurred vision during an exacerbative bout of temperature elevation and discomfort. Then another medical house officer, three months after admission, thought that there was a haziness of the disc, nasally, but that the fundi otherwise seemed negative. Previously, shortly after admission, the medical resident had made a note of the conjunctival injection and the redness and edema of the lids.

Ophthalmologic examination was requested 3½ months after admission, after which there were periodic consultations by several observers, and fundus drawings were made. It was found on this first examination (fig. 1) that both optic discs were equally normal in color and demarcation and structurally were normally full. The fovea of the left eye and the macular areas of both were distinguishable as such. In general, the retinopathy found in the left eye was similar

to, but not so advanced as, that observed in the right. Here, numerous fine to larger, superficial hemorrhages of all types were seen in the relatively avascular macular and peripheral retinal areas as well as in other places where the retinal circulation was not obviously abundant. These hemorrhages, furthermore, were in close proximity to capillaries and to the smaller venules and arterioles, especially the former. There was marked periphlebitis slightly temporal to, and in the far periphery above, the disc. Segmental periphlebitis on a lesser scale was observable in the extreme peripheries, chiefly in the temporal quadrants. The general impression of a severe vasculitis was heightened by the presence of somewhat deep retinal and more superficial choroidal, roundish, gray-white exudates, the distribution of which was more irregularly diffuse than that of the hemorrhages. A group of older, partially absorbed exudates in the macular area was situated so deeply that it was believed they had their origin in the relatively lush vascular areolar area of the choriocapillaris. The general ophthalmoscopic impression recalled previous observations of such diffuse disease entities as periarteritis nodosa and, less typically, dermatomyositis.

Subsequent examinations revealed progressive intensification, but on a more extensive scale, of the retinopathy just described; however, the changes in the left eye continued to be proportionately less marked than those in the right. The vasculitis became more widespread and progressed proximally toward the disc; hemorrhages and exudates became more numerous but there continued to be some absorption of those previously present. One large subhyaloid hemorrhage occurred superiorly in the right eye but was absorbed within a few weeks, and a large oval hemorrhage nearly the size of the disc appeared in the upper macular area in this eye. There occurred progressive obliteration of the lumen of the more peripheral retinal vasculature with complete replacement fibrosis manifested by yellowish-white connective-tissue cords traversing the original vascular channels and shading fairly abruptly into the still patent, more proximal vessels whether

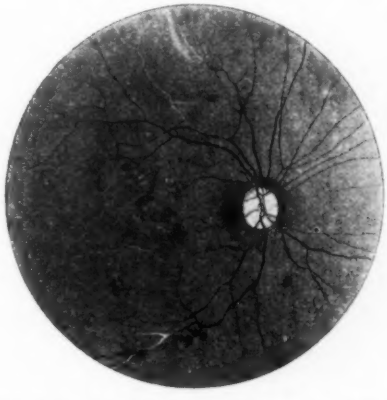


Fig. 2 (Koch and McGuire). O.D. drawing, June, 1939.

venous or anteriolar. There was primary optic atrophy in the right eye eight months after admission, when the second drawing was made (fig. 2) but this phenomenon still was in progress of development one month later in the left eye (fig. 3). The eyegrounds in general became mildly anemic in color.

Subjective ocular testing was not feasible because of the patient's discomfort and her lack of sustained coöperation, nor could additional drawings be made. As debasement of the general clinical findings progressed, further intensification of the described retinopathy occurred, and, although the changes in the left eye continued to lag somewhat behind those observed in the right, the conversion to fibrosed cords of previously normal vascular channels continued together with increasing optic-nerve atrophy and gradually decreasing hemorrhaging and exu-

dation. The retina became thinner, but the increase of diffuse, fine, granular, retinal pigmentation permitted no visualization of the choroid. Prior to death, light perception was lost in the right eye and was barely elicitable in the left. The media remained clear in each eye.

Discussion

Speculation on the central etiology in this case with its widespread clinical

Fig. 3 (Koch and McGuire). O.S. drawing, July, 1939.

manifestations remains speculation in the deplorable and unfortunate absence of post-mortem examination; however, it is of interest to consider the opinions of two groups of observers in this connection. Klemperer, Pollack, and Baehr, recalling the thesis of Morgagni that diseases reside in certain organs, point out that we recognize the interdependence and unity of certain organs to form organ and tissue systems, and that entities such as acute disseminated lupus erythematosus and diffuse scleroderma, among others, may reasonably be considered as systemic diseases of the connective-tissue system with fibrinoid degeneration of the collagenous fibers and ground substance. These authors, although granting the possibility that fibrinoid degeneration of collagen may result from hyperergic inflammation, do not believe that this type of degeneration always indicates a state of hypersensitivity. They feel that further investigation of the colloid system and its colloidal status must be made by biophysical and chemical methods.

The recent excellent review on the lupus-erythematosus concept by Stokes, Beerman, and Ingraham, Jr., stresses, on the other hand, the application of the "id" conception (tuberculids, syphilids, follicular "ids," *et cetera*) as that of allergic inflammation with its sequelae and homologies. Thus, it is suggested that "dissemination of a discoid or follicular erythematous lupus (a lupo-erythematid?) with the appearance of desquamative patches with follicular atrophy over other parts of the body, is simply an extension of the follicular 'id' beyond its conventional locus, under conditions affecting the general allergic state of the individual." Exacerbation and generalization may occur as the allergic base is broadened by some influence such as sulfonamide therapy or tuberculin skin testing or the physical allergen of actinic rays. If these allergic manifestations, or "id"-like processes, remain confined to the skin itself, the prognosis is not grave because of the well-known benignity of the disseminating discoid type of the disease. The reviewers then state: "*On the other hand,* in the hypersusceptible person—the infection-allergic type of individual, let us say—the epidermo-allergic or folliculo-allergic type of reaction that underlies the chronic discoid process may at a suitable provocation pass over (though only occasionally) into the field of vasculo-allergic manifestations and assume the far graver characteristics of the so-called acute disseminating type of the disease."

Thus, as they so succinctly point out: "The vasculo-allergic type of 'lupus ery-

thematosus' then, may be preponderantly local and cutaneous in its manifestations, or preponderantly systemic (fever, lymphadenopathy, leukopenia, absolute or relative, with or without thrombocytopenia, and with demonstrable vascular lesions, of the eyes, kidney and endocardium). It may be acute or chronic, or both. It may be combined with follicular 'id' lesions of discoid type and distribution, or not. The systemic vasculo-allergic lesions may come to notice first and dominate the picture to exitus." The reviewers strongly imply, moreover, that they are not in agreement with those dermatologists who believe that the absence of skin lesions is not uncommon and it is implied that a thorough search will not fail to reveal typical cutaneous lesions in this systemic disease.

In this connection, it is our opinion that early and thorough ophthalmoscopic examination is strongly indicated in all instances of "fever of unexplained origin" (one of the synonyms for acute disseminated lupus erythematosus) in pale, sickly, weak, asthenic women in their menstrual years. There also may be light sensitiveness, febrile episodes, with or without leucopenia, cutaneous petechiae, thinning hair, puffiness, and redness of the lids, arthritoid disturbances with relief of pain by salicylates but with no corresponding temperature decline, and pleural, endocardial, and pericardial signs and symptoms but with negative blood cultures.

Few males, and then only in the years between puberty and early middle age, develop this disease. Stokes and his co-reviewers as well as the Mayo Clinic group hold pessimistic views concerning the effect of treatment of this condition; however, the former have discussed cautiously the possible benefit to be derived from induced menopause as considered by Rose. Indiscriminate but well-intentioned chemotherapy as a cause of exacerbation of a concealed systemic focus of infection might reasonably be avoided to some extent if early ophthalmoscopic examinations were made routinely whenever this type of disseminated erythematosus was suspected. It is our opinion that, although elevation of systemic blood pressure may ensue because of the nephritis present, the ophthalmoscopic differentiation between, or the coexistence of, the lupus and the hypertension should not be impossible if the intraocular findings, as indicated in this report, are considered as vasculo-allergic manifestations of widespread systemic, diffuse collagen disease.

References

Kierland, R. R., Montgomery, H., Stickney, J. M., Keith, N. M., Slocumb, C. H., and O'Leary, P. A. Symposium on lupus erythematosus. Proc. Staff Meet. Mayo Clin., 1940, v. 15, Oct. 23, pp. 675-688.

Klemperer, P., Pollack, A. D., and Baehr, G. Diffuse collagen disease: Acute disseminated lupus erythematosus and diffuse scleroderma. Jour. Amer. Med. Assoc., 1942, v. 119, May 23, pp. 331-332.

Maumenee, A. E. Retinal lesions in lupus erythematosus. Amer. Jour. Ophth., 1940, v. 23, Sept., pp. 971-981.

Rose, E. Quoted by Stokes, *et al.*

Stokes, J. H., Beerman, H., and Ingrahm, N. R., Jr. The "lupus erythematosus" concept: An attempt at integration. Amer. Jour. Med. Sci., 1944, v. 207, April, pp. 540-549.

Supplementary references

Abramowicz, I., and Dulewicz, M. Changes in fundus of eye in acute lupus. Ann. d'Ocul., 1933, v. 170, July, pp. 599-602.

Banks, B. M. Lupus erythematosus: Is there a common denominator in scleroderma, derma-

tomyositis, disseminated lupus erythematosus, Libman-Sacks syndrome and polyarteritis nodosa? New Engand Jour. Med., 1941, v. 225, Sept. 18, pp. 433-444.

Fox, R. A. Disseminated lupus erythematosus—allergic disease? Arch. Path., 1943, v. 36, Sept., pp. 311-315.

Fry, W. E. In discussion of Steele, W. H. Papilledema in acute disseminated lupus erythematosus. (Trans. College of Physicians of Philadelphia, Sect. on Ophth.) Arch. of Ophth., 1943, v. 30, July, p. 149.

Guion, C. M., and Adams, E. C. Six autopsied cases of disseminated lupus. Amer. Jour. Med. Sci., 1943, v. 205, Jan., pp. 33-41.

Klauder, J. V., and Ellis, Van M. Effective treatment of lupus erythematosus and exudative retinitis with a gold compound. (Trans. College of Physicians of Philadelphia, Sect. on Ophth.) Arch. of Ophth., 1939, v. 21, May, pp. 893-894.

MacMahon, H. E. Lupus erythematosus: Visceral manifestations of disseminated lupus. Bull. New England Med. Center, 1941, v. 3, Oct., pp. 252-258.

Semon, H. C., and Wolff, E. Acute lupus erythematosus, with fundus lesions. Royal Soc. Med. Proc., 1934, v. 27, pp. 153-157.

NUTRITIONAL AMBLYOPIA IN AMERICAN PRISONERS OF WAR LIBERATED FROM THE JAPANESE

SAMUEL M. BLOOM, MAJ. (MC), A.U.S., EARL H. MERZ, MAJ. (MC), A.U.S., AND WILLIAM WICKHAM TAYLOR, CAPT. (MC), A.U.S.
Phoenixville, Pennsylvania

The purpose of this paper is to present the clinical picture of American soldiers liberated after an extended confinement in Japanese prison camps under conditions of severe malnutrition. The study was done on 33 soldiers captured in April and May, 1942, on Bataan and Corregidor, and liberated in early 1945. The development of early symptoms and findings was observed by one of us (S. M. B.) while a prisoner in Cabanatuan. The final and residual findings were observed by the other two collaborators while the patients were hospitalized in an Army eye center in the United States. During the period from liberation to arrival at this Eye Center, the patients had received an adequate diet and supplemental vitamin therapy and had returned to approximately their normal weight.

OBSERVATION OF PRISONERS OF WAR IN THE PRISON CAMP

Beginning in May, 1942, the survivors of the American forces of Bataan and Corregidor were subjected to living conditions which led to malnutrition, various vitamin deficiencies, and starvation in the Japanese prison camps in the Philippines.

In the main, the diet consisted of about 300 gm. of polished rice plus a thin soup made of low-grade vegetables and weeds. Negligible amounts of fruit were occasionally furnished. Meat was almost completely lacking. Rarely, one pig would be furnished for a group of 2,500 men. After dressing and cooking, about all that would appear in the soup would be a bit of the hide and a few shreds of meat.

During the first four months of imprisonment, the men developed beriberi (both the wet and dry types), scurvy, pellagra, ariboflavinosis, and xerophthalmia, to mention a few of the clinical syndromes apparent. Naturally, the picture was that of a mixed avitaminosis in most cases, with one or other of the manifestations predominating. In addition, malaria, dysentery (amebic and bacillary), and diphtheria affected many. Of about 6,500

in Cabanatuan, 2,700 men died in the first year.

Blurring of vision began insidiously. It was first reported in September, 1942; that is, after about four months of starvation diet. The impairment of vision was described by most of the patients as an intermittent fading, more marked in bright sunlight. This process was gradual, and went unnoticed by many. After two to four weeks, retrobulbar pain and burning sensation in the eyes appeared in attacks during the later afternoon of bright sunny days, or during the early evening. These attacks were accompanied by photophobia and lacrimation. At that time, examination usually revealed no external gross alteration of the eyes; but in a few instances, mild injection of the conjunctiva was present. No visual test charts were available nor materials with which to make them; no lenses, no ophthalmoscopes, and practically no medicines, so that examination and treatment were extremely limited.

In October, 1942, the attacks of burning in and behind the eyes became more marked. It was then that the cornea was noted to be dry and roughened. After another day or two, superficial ulcers appeared. These were mostly round or oval in shape, over the pupil or lower half of the cornea, and usually single. Circumcorneal injection became evident. Unfortunately, no fluorescein or other staining drug was available at the time. In most cases, there was little infiltration of the cornea. Small amounts of cod-liver oil were obtained, and it was found that the ulcers healed after 4 to 10 days of its administration. However, the impaired vision persisted and, in most cases, progressed. A few of the corneal ulcers went on to perforation, or were complicated by hypopyon and iritis.

In November, 1942, a change of Japanese administration brought an increase in the ration. Rice was increased to 400 gm., meat to 50 gm., and squash and comotes (a variety of sweet potato) were added. For the eye patients, 4 oz. of evaporated milk, and 4 oz. of carabao liver, when available, were added to the diet. The latter items seemed to have the most effect in arresting the development of corneal ulcers and in healing the manifestations of ariboflavinosis. By this time, also, a visual-test chart was made and batteries for an ophthalmoscope were obtained. Examination revealed pallor of the disc in the region of the papillo-macular bundle. Vision was reduced to 10/200 on the average, by December, 1942, and usually remained stationary thereafter, although in some cases, a slow decline continued. Central vision was most affected. Fields showed central and cecocentral scotomas, with moderate constriction of the peripheral fields.

At this point, one of us (S. M. B.) was transferred to Santo Tomás, a camp for Allied civilian internees. Here an opportunity arose to observe the effect of early treatment in conditions similar to those afore described. These people had fared better up to that time by being allowed to receive or purchase food from the neutrals and Filipinos outside. They were not dependent on the Japanese ration, which was just as inadequate as at Cabanatuan. However, the Japanese closed all traffic with outside sources on February 1, 1944, and by May, patients were complaining of photophobia, retrobulbar pain, and diminution of vision, particularly in bright light. Small supplies of thiamin chloride were available from the American Red Cross shipment of August, 1943 (delivered to the internees January, 1944), so that we were able to give 25 mg. daily for two to three weeks to affected individuals. This dosage served to check

the progress of the disease. Multiple vitamins were given along with injections of the thiamin. A patient who had lost 80 pounds in 12 months at Fort Santiago (Political Military Prison) and who had developed beriberi as well as a diminution of vision to 10/200 with central scotomas, made a fair recovery over a period of eight months during which he was treated as has been outlined. By November, 1944, he was able to read large print and his own handwriting. His vision returned to 20/70. In December, 1944, because of the marked starvation (the diet was down to 200 gm. of polished rice daily), his vision began to deteriorate again.

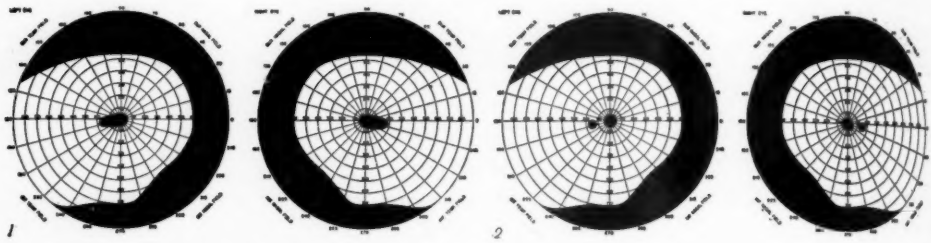


Fig. 1. (Bloom *et al.*). Central fields in a typical case—0.5° target.
Fig. 2. (Bloom *et al.*). Central fields in a typical case—1° target.

In Santo Tomás, colored visual fields were charted. Patients showed earliest changes in the blue field; then changes in the red and green fields, enlargement of the blind spot, constriction of peripheral fields; later, central or cecocentral scotomas became evident.

Observation of liberated prisoners in the eye center

To give a detailed report on each case studied at this Eye Center would be unnecessary repetition, for all the cases fall into a uniform pattern in their essential findings. These data will be presented in the chart, showing the minor variations in each case.

Typical case. The patient entered the Hospital with complaints of: (1) decreased vision in both eyes, (2) inability to see an object when using central vision, (3) burning and pain in the extremities.

On admission to this Hospital, his appearance was that of a well-developed and well-nourished man. (His history has been related.) The physical examination performed by the Medical Service showed no abnormalities or variation from normal. Neurologic examination was entirely negative except for: (1) peripheral neuritis and (2) optic atrophy, bilateral. Laboratory work consisted of: (1) basal-metabolism rate, (2) electrocardiogram, (3) blood chemistry, (4) electro-encephalogram, (5) cephalin flocculation, (6) X ray of lungs and heart, (7) routine urinalysis, (8) blood count, (9) serum reactions. All of these tests were normal. Stool examination revealed intestinal parasites.

The eye examination was as follows: The external examination revealed normal lids, conjunctiva, sclera, and cornea. The lacrimal apparatus was patent, and tactile tension normal. External ocular movements were full, and the pupils reacted to light and accommodation. No lacrimation or photophobia was present. On slitlamp examination, the cornea appeared normal, with no increase in limbal vascularization, no degeneration, no thinning, and no xerosis. The iris stroma, lens, and anterior vitreous were normal

throughout. The anterior chamber was of normal depth; the aqueous ray was absent. No cells were seen. With well-dilated pupils, the ophthalmoscopic examination showed clear media. No elevation nor abnormal excavation of the optic-nerve head was seen. The edges were clearly defined and distinct. The temporal portion of the disc showed a definite pallor, whereas the nasal portion was relatively normal. The vascular tree was normal, and the periphery of the fundus revealed no pathologic lesions. The macular area appeared normal in approximately 60 percent of the cases and mottled in 40 percent. Vision in each eye was 20/200, not correctable. The peripheral fields showed mild, generalized constriction, but were not remarkable. The central fields showed a central scotoma of 5 to 8 degrees, with a 1-degree target under good illumination, and a centrocecal scotoma, either absolute or relative, with a 0.5-degree target. The scotomas were larger for colors than for white.

A diagnosis was made of optic atrophy secondary to nutritional deficiency.

Treatment consisted of a high-vitamin, high-caloric diet, supplemented by daily administration of six multivitamin capsules, thiamin (50 mg., intramuscularly), and riboflavin (10 mg.). This treatment was instituted for a 60-day period. After this course of treatment, a reëxamination showed no change in any case.

Comment

The description given is that of a typical case, and the following discussion will deal with the variations.

Cornea. Five patients showed small corneal scars resulting from ulcers that occurred in 1942, and one showed a complete leucoma following a perforating ulcer suffered at that time. All other corneas were clear.

Discs. The color of the discs varied from a minimal temporal, to almost complete pallor, but the vast majority showed only mild temporal pallor. The most striking feature was the lack of correlation between the visual acuity and the extent of the optic atrophy.

Maculas. The maculas, as has been stated, were normal in 60 percent of the cases, while 40 percent showed macular mottling and loss of foveal reflex.

Central fields. The central fields (figs. 1, 2) varied only in size and in the density of the scotomas, the latter depending on the severity of the condition.

Vision. The vision varied from 20/40 to 2/200 and varied directly with the density of the scotoma.

Extrinsic factors. As seen in the chart, there were many factors which had a definite influence on the final vision retained. These factors were as follows: (a) Patients having the most severe cases of malnutrition died; at this Center we dealt with the less severe cases. (b) Of this group, the men from Bataan seemed to have suffered more than the men captured on Corregidor because of the lack of supplies to the Bataan force prior to capture. They showed definite signs of malnutrition and early beriberi before surrendering, but had no eye complaints that we know of. (c) The diets of the various prison camps played a paramount role in determining the end result. At Bilibid and Cabanatuan, the diets were most deficient, consisting mostly of rice and soup from cancong weed. Here the inmates showed the most marked pathologic changes. At the other extreme, prisoners at some camps in the southern portion of Japan proper showed much less change because their rice diet was supplemented with fish, fresh fruit, and occasional meat. It is interesting to note that three patients with no pathologic eye findings (not included

TABLE 1

THE FINDINGS IN 33 AMERICAN SOLDIERS LIBERATED FROM THE JAPANESE

	Cornea	Nerve head	Fundus	Peripheral Fields	Central Fields	Vision	Diet Supplement	Camps	Onset of Visual Symptoms
1.	Normal	Mild temp. pallor	Macular mottling	Normal	Central scotoma	20/200 20/50	No vitamins Mukden diet good	Cabanatuan Mukden	Nov. 1942
2.	Normal	Temp. pallor	Normal	Mild constrict.	Centro-cecal scotoma	20/70 20/70	Few vitamins	Wawa	July 1942
3.	Macula OD Normal OS	Mild temp. pallor	Normal	Mild constrict.	Central scotoma	20/200 8/200	Few vitamins	Death march Cabanatuan Japan	Oct. 1942
4.	Normal	Mild temp. pallor	No foveal reflex	Normal	Central scotoma	20/100 20/100	Few vitamins	Cabanatuan	Oct. 1942
5.	Normal	Mild temp. pallor	No foveal reflex	Normal	Centro-cecal scotoma	20/50 20/200	Few vitamins Davao diet good	Death March Davao Korea	July 1942
6.	Normal	Mild temp. pallor	No foveal reflex	Normal	Centro-cecal scotoma	20/100 20/100	Few vitamins	Cabanatuan	Jan. 1942
7.	Nebula OD Leucoma OS	Temp. pallor OD Fundus not seen	Normal OD	Normal	Centro-cecal scotoma	20/100 H.M.	Thiamin Nov. 1942 Mukden diet good	Death March Cabanatuan Mukden	July 1942
8.	Normal	Temp. pallor	No foveal reflex	Mild constrict.	Central scotoma	20/200 20/200	Few vitamins	Cabanatuan Bilibid Fort McKinley	Sept. 1942
9.	Normal	Temp. pallor	No foveal reflex	Normal	Central scotoma	20/100 20/200	Thiamin 1942	Cabanatuan Korea Japan	Sept. 1942
10.	Normal	Mild temp. pallor	Normal	Normal	Centro-cecal scotoma	20/70 20/100	Few vitamins	Cabanatuan	Nov. 1942

TABLE 1 (Continued)

	Cornea	Nerve head	Fundus	Peripheral Fields	Central Fields	Vision	Diet Supplement	Camps	Onset of Visual Symptoms
11.	Normal	Mild temp. pallor	Normal	Mild constrict.	Centro-cecal scotoma	20/70 20/200	Vitamins in Hosp.	Cabanatuan Bilibid Hosp. July 1944 Japan	Nov. 1942
12.	Nebula OD Normal OS	Marked temp. pallor	Normal	Normal	Central scotoma	20/100 20/200	No vitamins	Cabanatuan Japan Nov. 1942	Nov. 1942
13.	Nebula OD Normal OS	Temp. pallor	Normal	Normal	Small central scotoma	20/200 20/100	None	Cabanatuan Japan May 1943	Jan. 1943
14.	Normal	Mild temp. pallor	Normal	Mild constrict.	Central scotoma for color	20/40 20/40	Five months of vitamins	Bilibid Cabanatuan Japan 1944	Mar. 1943
15.	Nebula OD Normal OS	Moderate temp. pallor	Normal	Normal	Central scotoma	20/100 20/100	Thiamin in Hosp. in Bilibid	Cabanatuan Bilibid Hosp. Japan 1943	Oct. 1942
16.	Normal	Temp. pallor	Normal	Mild constrict.	Central scotoma	20/200 20/200	None	Cabanatuan	Oct. 1942
17.	Normal	Temp. pallor	Macular mottling	Normal	Central scotoma	6/200 4/200	None	Cabanatuan	Oct. 1942
18.	Normal	Compl. pallor	Macular mottling	Mild constrict.	Central scotoma	5/200 10/200	None	Bilibid	Jan. 1942
19.	Normal	Temp. pallor	Normal	Normal	Central scotoma	20/200 20/200	None	Cabanatuan	Aug. 1942
20.	Normal	Compl. pallor	Normal	Normal	Central scotoma	1/200 1/200	Six months of thiamin	Cabanatuan Bilibid	Oct. 1942
21.	Normal	Mild temporal pallor	Normal	Normal	Central scotoma	L.P. L.P.	None	Cabanatuan Bilibid	Sept. 1942

TABLE 1 (Continued)

	Cornea	Nerve head	Fundus	Peripheral Fields	Central Fields	Vision	Diet Supplement	Camps	Onset of Visual Symptoms
22.	Normal	Temp. pallor	Macular mottling	Mild constrict.	Central scotoma	3/200 3/200	None	Cabanatuan Bilibid	July 1942
23.	Nebula OD Normal OS	Temp. pallor	Normal	Mild constrict.	Centro-cecal scotoma	20/100 10/200	Few vitamins	Cabanatuan Bilibid	Sept. 1942
24.	Normal	Temp. pallor	Normal	Normal	Central scotoma	20/200 10/200	None	Cabanatuan	Dec. 1942
25.	Normal	Temp. pallor	Normal	Mild constrict.	Centro-cecal scotoma	20/200 10/200	None	O'Donnell Cabanatuan	Nov. 1942
26.	Normal	Temp. pallor	Mac. mottling OD Normal OS	Normal	Centro-cecal scotoma	20/200 10/200	None	Cabanatuan Bilibid	Oct. 1942
27.	Normal	Temp. pallor	Normal	Normal	Central scotoma	10/200 10/200	Few vitamins	Cabanatuan	Oct. 1942
28.	Normal	Temp. pallor	Normal	Normal	Central scotoma	5/200 10/200	None	Cabanatuan	Oct. 1942
29.	Normal	Temp. pallor	Macular mottling	Mild constrict.	Centro-cecal scotoma	1/200 2/200	None	Cabanatuan Davao	Oct. 1942
30.	Normal	Temp. pallor	Normal	Normal	Central scotoma	20/200 8/200	None	Cabanatuan	Oct. 1942
31.	Normal	Moderate temp. pallor	Normal	Normal	Centro-cecal scotoma	5/200 5/200	None	Cabanatuan Bilibid	Oct. 1942
32.	Normal	Temp. pallor	Macular mottling	Mild constrict.	Relative central scotoma	20/100 20/70	Few vitamins	O'Donnell Cabanatuan Japan	Oct. 1942
33.	Normal	Temp. pallor	Normal	Mild constrict.	Central scotoma	20/200 20/100	Few vitamins	Cabanatuan	Oct. 1942

in this report), were imprisoned in camps where the diet approached normal. In most camps, the rice served was polished. However, in at least one instance, the rice polisher broke and unpolished rice was served for two months. A definite improvement in the condition of the men resulted during this time. On returning to the diet of polished rice, they suffered a recurrence of former symptoms. The men state that the prisoners who refused to eat the cancong soup, and those bartering their food for cigarettes, suffered more severely than others.

Another important factor was the presence of severe malaria, dengue fever, and dysentery (bacillary and amebic). These diseases caused marked debility and anorrhexia which prevented the ingestion of what little food was allowed them.

From time to time, the men were able to supplement their diets with vitamins obtained in various manners, and a temporary improvement in their condition was noted at such times. The most striking example of this was seen when a marked improvement in symptoms among all prisoners followed the administration of a small amount of Red Cross supplies in December, 1943.

Discussion

A group of patients is presented that has had an extremely unusual and unfortunate experience. These men have been under conditions of malnutrition and avitaminosis for a long period of time and give accurate histories of severe loss of weight, extreme weakness, and symptoms of diseases due to lack of food and vitamins. Since liberation, they have all been on diets high in calories and rich in vitamins, with recovery from all symptoms except those referable to nerves and eyes.

During the onset and development of amblyopia (from May, 1942, to November, 1942), their diet consisted of from 200 to 400 gms. of polished rice a day and watery soup made from cancong weed. Later, small amounts of other vegetables, fruit, fish, and meat were added, but the diet was always far from adequate. Polished rice is very low in thiamin (trace to 0.5 μmg. per gm.), and the cancong soup contained a negligible amount. Two hundred to 400 gm. of rice furnish approximately 700 to 1, 400 calaries, so that the total caloric intake per day was probably 900 to 1,600 calories. Not only was the caloric intake low, but the ratio between thiamin ingested and total amount of calories consumed was also abnormally low. Cowgill,[1] in 1934, showed that a definite relationship should exist between total caloric intake and thiamin ingested, and that when this is not normal, symptoms of deficiency developed. Besides this abnormal relationship there was another. In "Vitamin therapy" by Gordon and Severinghaus,[2] it is stated that the thiamin requirement of man is dependent on the proportion of fat to carbohydrate in the diet. Fat has a thiamin-sparing action, whereas carbohydrate increases the need for thiamin. On looking at the diet described, we find rice to have 79.3-percent carbohydrate, 0.26-percent fat, 7.1-percent protein; therefore, the need for thiamin is very apparent. In 1942, at Mayo Clinic, Williams, Mason, Smith, and Wilder[3] gave the requirements of thiamin for man. They stated that, on .07 mg. thiamin per 1,000 calories, patients had weight loss and noted increasing weakness. They also found that the minimal daily requirements of thiamin for man was between 0.22 and 0.50 mg./1,000 calories providing CHO/fat ratio was normal. The diet these men were on had insufficient thiamin requirements, had an

abnormal thiamin/caloric ratio, and an abnormal fat/CHO proportion which necessitated increased thiamin. This all shows that a definite thiamin deficiency was present.

Another observation to be made is the similarity of our findings to those of Carroll's[4,5] and Johnson,[6] who reported cases of tobacco-alcohol amblyopia which they believed due to thiamin deficiency. In both conditions, we see defective vision, central or cecocentral scotomas, normal peripheral fields, and temporal pallor of the optic-nerve head. In one paper,[5] Carroll suggests that the amblyopia could be a "manifestation of a deficiency condition without toxic elements" or could be due to "toxic action of tobacco on malnourished cells." He further suggests that when B_1 is added, the nutrition of the damaged cells, or perhaps their axons, improves, and the injurious agent is no longer injurious. He also shows improvement in vision and fields on thiamin therapy. Our findings sustain the first premise, for no toxic element was apparently concerned. In another paper,[4] Carroll shows a case in which the eye findings were almost identical to ours and which unquestionably improved on thiamin therapy.

Thiamin therapy was tried in all our cases but the results were poor. It is believed they were thiamin deficient so long that irreversible changes had taken place in the optic nerve. The peripheral neuritis in the extremities was not relieved, probably for the same reason. However, some of the patients not included in this report, because they were not blind, improved under parenterally administered thiamin therapy when given in early stages of the deficiency. Sufficient amounts were not available to treat all prisoners.

It is of interest to note that Moore[7] describes a syndrome of misty vision, photophobia, and optic atrophy associated with glossitis, perleche, and itchy, scaly scrotum along with neuritic changes which closely resembled this disease in early stages. These patients were African sugar-plantation workers whose diet was very deficient. After the pellagra and ariboflavinosis cleared, vision, as well as symptoms of peripheral neuritis, remained unimproved. The symptoms and final end results closely resemble those experienced in the prison camps.

It is of possible importance that the men in our prisoner-of-war series claimed better vision in dim light, as in evenings, than in ordinary daylight. This is contrary to what one would expect in vitamin-A deficiency and, although adequate amounts of cod-liver oil were available and given, it failed to arrest the declining vision, which was evidence that some other factor was responsible. However, the vitamin A did result in healing of the corneal ulcers. The central scotomas, photophobia, and lacrimation were responsible for the poor vision in bright light. At night, the uninvolved retina would be expected to function more or less normally.

Summary

The early eye findings in American soldiers while in Japanese prison camps and residual findings in some of these men after liberation have been presented. The following conclusions are drawn:

1. Malnutrition due to a deficient diet can cause an optic atrophy manifested by defective vision, central or centrocecal scotomas, and pallor of the nerve head.

2. The deficiency seems to be due to a lack of vitamin B_1, since the diet, in every case, was highly deficient in this vitamin; the symptoms occurred coincidentally with beriberi; and the symptoms were re-

lieved by thiamin when administered in the early stages of the deficiency.

3. If treatment is not instituted early enough, the condition becomes irreversible, as witnessed by the lack of improvement after administration of intensive vitamin therapy at this Center.

4. The loss of vision and the size of the central scotomas were not in direct proportion to the amount of optic atrophy seen.

5. The appearance of the disc varied from minimal to complete atrophy, with the vast majority of eyes showing mild temporal pallor.

6. The maculas had a normal appearance in 60 percent of the cases and a mottled appearance with loss of the foveal reflex in the remainder.

7. The nerve involvements—peripheral neuritis and optic atrophy—were the only residual abnormal findings made at this Center on patients who had suffered severe malnutrition over a period of years.

Valley Forge General Hospital.

References

[1] Cowgill, G. R. Vitamin B requirement of man. New Haven, Conn., Yale University Press, 1934, p. 110.

[2] Gordon and Severinghaus. Vitamin therapy. Chicago, Year Book Publishers, Inc., 1942.

[3] Williams, R. D., Mason, H. L., Smith, B. F., and Wilder, R. M. Induced thiamin deficiencies and thiamin requirements of man. Arch. Int. Med., 1942, v. 69, May, p. 721.

[4] Carroll, F. D. Recurrence of tobacco-alcohol amblyopia. Amer. Jour. Ophth., 1945, v. 28, June, p. 636.

[5] ——. Tobacco-alcohol amblyopia. Amer. Jour. Ophth., 1944, v. 27, July, p. 713.

[6] Johnson, L. V. Alcohol-tobacco amblyopia treated with thiamin chloride. Arch. of Ophth., 1939, v. 21, April, p. 602.

[7] Moore, S. F. Retrobulbar neuritis with avitaminosis. West African Med. Jour., 1937, v. 9, June, pp. 35-40.

CHANGES IN THE ANGIOSCOTOMAS ASSOCIATED WITH THE ORAL ADMINISTRATION OF EVIPAL*

AUSTIN I. FINK, M.D.†
Brooklyn, New York

INTRODUCTION

For some time ophthalmologists have been concerned with the question as to whether barbiturates are contraindicated in the treatment of patients with glaucoma. This concern has derived to a great extent from the fact that large doses of barbiturates have been known to produce a dilation and to increase the permeability of the cerebral blood vessels and capillary bed.[1, 2]

With a suitable method, one could study the effect of an orally administered barbiturate upon the retinal vascular system. Angioscotometry was chosen as a suitable method for this experiment, since changes in the normal angioscotoma are assumed to represent alterations in the functions of the retinal perivascular space.

METHODS AND MATERIAL

The word "angioscotoma" signifies a "defect in the visual field related in form to the pattern of distribution of the retinal vessel tree."[3] These shadows (after extensive research) have been interpreted as arising because of modifications of the retinal perivascular spaces and in the retinal synaptic junctions.[4]

Technique. The scotoma was mapped according to the method advocated by Evans.[5] The defects in the visual fields could thus be studied both qualitatively and quantitatively.

The Evans stereocampimeter and charts were used. Monocular fixation was employed throughout the experiment. The diameter of the spherical, white test object used was in all cases 0.4 mm. (illumination of the test chart was approximately 15 foot-candles). The blind spot of Mariotte was outlined. Then the two main superior angioscotomas were plotted by moving the object from seeing to blind, care being taken at all times to move the test object at right angles to the border of the defect.

Subjects. Ten studies were carried out on 10 different subjects, 9 female and 1 male. The ages of the subjects ranged from 21 to 26 years. All known causes for alteration of the angioscotoma were carefully eliminated. Each subject was found to be in good health.

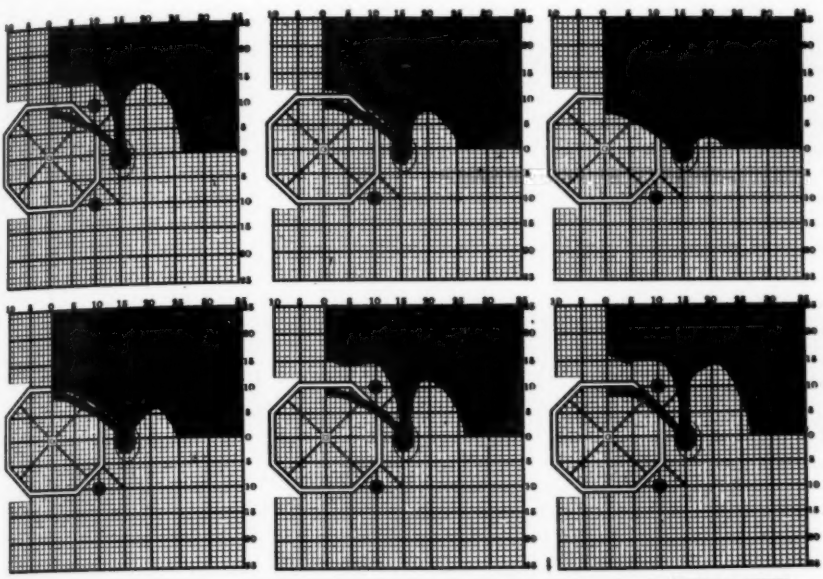
Procedure. The subjects rested for approximately ten minutes before any mapping was begun. During this period the pulse and blood-pressure values were recorded. The subjects were familiarized with the apparatus and instructed to respond either by tapping with a pencil or by saying "gone" to indicate the disappearance of the test object. The first map or control was then plotted. The subject then took orally a tablet containing 4 gr. of evipal.‡ This particular drug was employed because evipal is a rapidly acting barbiturate. Four grains is an average

* From the Department of Ophthalmology of the Long Island College of Medicine and the Long Island College Hospital. Presented at the 15th scientific meeting of the Association for Research in Ophthalmology, Inc., at San Francisco, July 2, 1946.

† Now Lieut. (MC), A.U.S.

‡ Evipal is N-methylcyclohexenylmethyl barbituric acid.

adult hypnotic dose.[1] A second chart was plotted 30 minutes after ingestion of the tablet in order to allow time for beginning absorption. The pulse and blood-pressure values were again recorded. This same technique was employed at 15- to 20-minute intervals until the control stage was once again reached.



TIME	B. P.	PULSE	SCOTOMA-UNITS
7:50	102/74	78	211
8:20	104/74	78	260
9:10	102/74	76	286
9:30	104/74	78	266
9:40	106/74	78	221
9:50	104/72	78	211

Fig. 1 (Fink). Angioscotomas plotted to show the effects on a subject (C. M.) after oral administration of evipal.

Observations

The accompanying charts, table, and graph illustrate the observations made with the subjects. A widening of the angioscotoma was associated with the oral administration of evipal in 8 of the 10 subjects. The other two showed no demonstrable alteration of the scotoma. There was no change in the area of the blind spot. Pupillary changes were not detectable by available methods. The first effects of the drug were noted from 30 to 45 minutes after the barbiturate had been taken. The average time was 35 minutes. Maximum effects were obtained from 45 to 105 minutes following ingestion. The average time was 70 minutes. The effect was lost in 90 to 205 minutes after oral administration, the average time being 149 minutes.

No subjective sequelae, such as psychic depression, were noted in any of the subjects. The effect on the blood-pressure

and pulse rate did not vary significantly so far as could be observed.

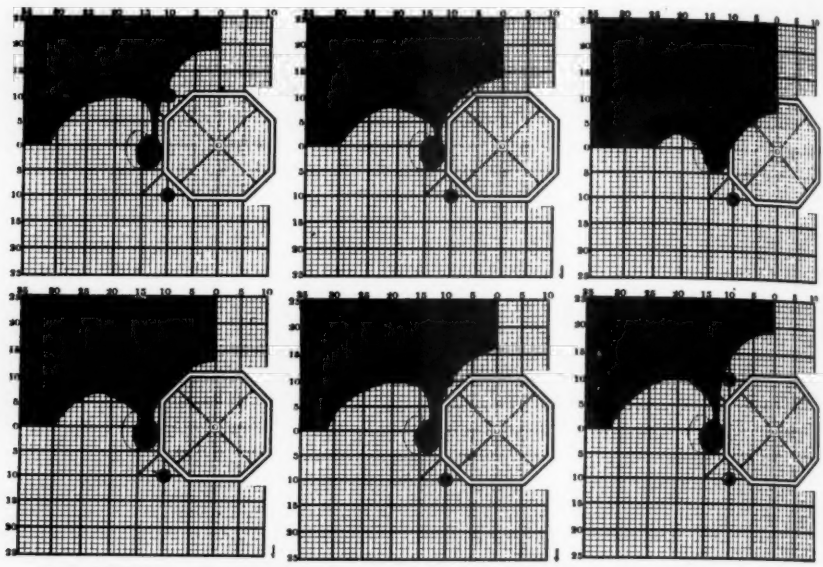
Comment

In attempting to evaluate what was observed in this experiment, it will be necessary to state what is thought to be the origin of the alteration of any angioscotoma.

The influencing factors are thought to be:

1. Anything that would interfere with the conductivity at the synaptic junctions, because in the presence of deleterious agents the synaptic junctions may act as a fuse to protect the rod-and-cone layer (neurogenic or nerve-fiber-bundle hypothesis).[5]

2. The disturbance of the normal physiology of the retinal perivascular system (angiogenetic or perivascular-space hypothesis).[5]



TIME	B.P.	PULSE	SCOTOMA UNITS
8:00	140/90	72	200
8:50	140/88	70	242
9:45	140/84	66	292
10:25	136/86	68	250
11:05	138/82	72	216
11:25	138/86	68	200

Fig. 2 (Fink). Angioscotomas plotted to show the effects on a subject (M. N.) after oral administration of evipal.

3. The autonomic nervous system which relates the first hypothesis to the second.[5] (Basic studies have been duplicated over the world by many workers and have been found in agreement.)

Evidence has been found in the literature to suggest that possibly each of the foregoing factors, in itself, may be con-

TABLE 1

APPEARANCE AND DURATION OF CHANGES IN THE SCOTOMA PRODUCED BY EVIPAL

Subject	First Change	Max. Effect	Effect Lost
	min.	*min.*	*min.*
P.H.	30	75	150
A.M.	0	0	0
C.M.	30	80	120
W.B.	35	55	170
A.G.	30	80	160
M.B.	30	60	140
A.F.	45	45	90
G.L.	30	60	160
J.B.	0	0	0
M.N.	50	105	205
Average	35	70	149

sidered as a partial explanation as to why the alterations of the angioscotomas took place in this experiment:

1. Microscopic sections of the brain from fatal cases of barbiturate poisoning have shown "a swelling or tumefaction of the ganglion cells."[6] This observation would lend support to that part of the neurogenic hypothesis.

2. In the introduction of this paper, it was stated that large doses of barbiturates have been known to produce a dilation and increase the permeability of the cerebral blood vessels and capillary bed.[1, 2] It would not be unreasonable to assume that this dilation and increased permeability would alter the physiology of the perivascular spare. This observation would then add support to the angiogenetic or perivascular-space hypothesis.

3. In studying the effects of evipal on the parasympathetic nervous system, Emelin has noted that "the effects are very similar to those caused by atropine. Evipal diminishes the responses obtained through a stimulation of the cholinergic nerves. It also counteracts the muscarine-like effects of acetyl-choline."[7, 8] The parasympathetic nervous system, it seems,

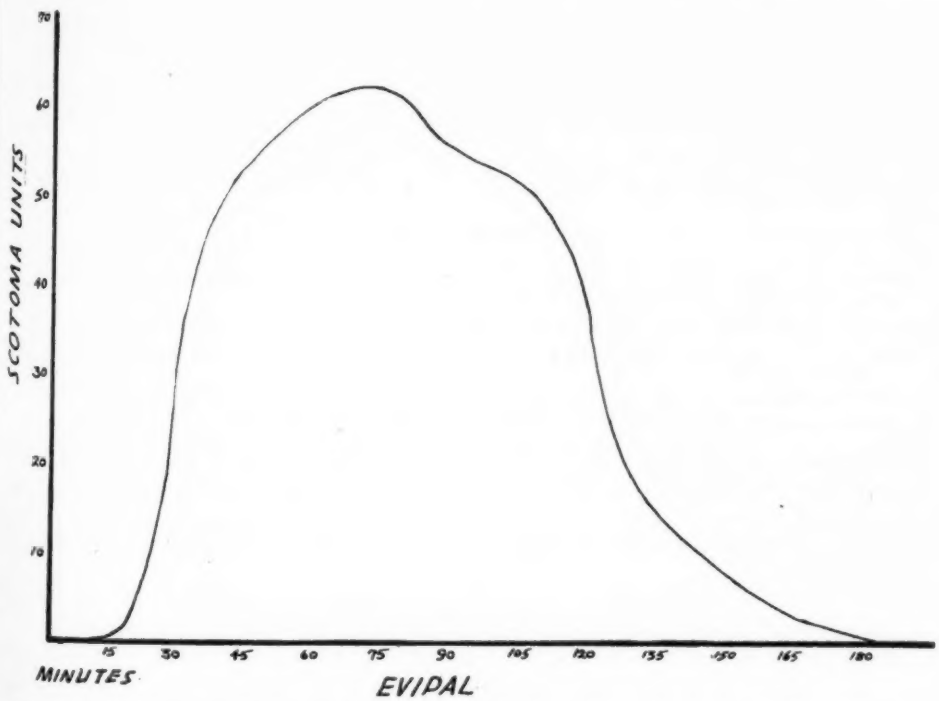


Fig. 3 (Fink). Graph illustrating the effect of evipal administration, expressed in scotoma units.

also exerts its influence to bring about the changes of the angioscotoma.

In summarizing, one might say that any one, or a combination of, the three pieces of evidence just presented might account for the alterations of the angioscotoma found in this experiment. Doubtless there are other mechanisms.

It will be remembered that 2 of the 10 subjects did not exhibit any change in the angioscotoma following the ingestion of evipal, whereas others showed a marked alteration of the central visual field. This seems in accordance with variations found in different patients when barbiturates are employed clinically. Some show no response; others are markedly depressed or even exhibit excitation.

On a controlled series of five of the subjects, an experiment was carried out, in which capsules containing 4 gr. of lactose (milk sugar) were administered orally. The subjects did not know that the capsules merely contained a placebo. The purpose of the control was to ascertain whether a psychologic factor was present and helped to cause the alterations in the angioscotomas occurring after the subjects ingested evipal. The method, technique, and procedure employed were identical with those used for the evipal studies. The results demonstrated that, in the series of five subjects, no alteration of the angioscotoma was recognized.

Conclusions

Under the conditions of these experiments and in the subjects tested the following conclusions were drawn:

1. The oral administration of 4 gr. of evipal was associated with a widening of the angioscotoma in 8 of 10 subjects. The other two showed no recognizable change.

2. Administration of a placebo containing 4 gr. of lactose to five of the subjects of the evipal series produced no alteration of the angioscotoma.

3. One might ascribe the associated effect of evipal on the normal angioscotoma as related to changes in: (a) the perivascular space functions; (b) conductivity of the retinal neurons and synaptic junctions; and (c) the parasympathetic nervous system.

The author wishes to express his sincere appreciation to Dr. John N. Evans for his guidance and encouragement during the preparation of this paper.

References

[1] Goodman, L., and Gilman, A. The pharmacological basis of therapeutics. New York, The Macmillan Company, 1941, p. 133.
[2] Marx. Jour. Pharm. and Exp. Therap., 1931, v. 41, p. 483.
[3] Evans, J. N. A preliminary report of the retinal vessel scotoma. Amer. Jour. Ophth., 1926, v. 9, Feb., pp. 118-119.
[4] ———. Angioscotometry. Amer. Jour. Ophth., 1926, v. 9, July, pp. 489-506.
[5] ———. Clinical scotometry. New Haven, Conn., Yale University Press, 1937.
[6] Hassin, G. B. Cerebral changes in fatal cases following treatment with barbital, soluble barbital U.S.P., insulin and metrazol. Arch. Neur. and Psychiat., 1939, v. 42, Oct., p. 679.
[7] Emelin, N. The effect of evipal on certain cholinergic organs. Schweiz. Med. Woch., 1940, v. 70, Dec., p. 1216.
[8] ———. Evipal and the parasympathetic nervous system. Acta. Physiol. Scandanav., 1941, v. 2, pp. 289-310.

Discussion

Dr. Fink (closing): One thing that was revealed to me was the fact that evipal had any connection with the autonomic nervous system. At present, angioscotometric studies are being carried out in our department on homatropine and atropine which should lend support to this observation.

THE ROLE OF LENS SUBSTANCE IN EXPERIMENTAL GONORRHEAL IRITIS*

MAURICE J. DRELL, M.D.
Seattle, Washington
MARJORIE BOHNHOFF, S.B., AND C. PHILLIP MILLER, M.D.
Chicago

INTRODUCTION

In the course of studies[1, 2, 3] on experimental gonorrheal iritis in rabbits, it was noted that the infection was more severe and more likely to become chronic in eyes in which the lenses had been traumatized at the time of inoculation. The present study was undertaken in an effort to explain this observation and to evaluate the role played by lens substance in the experimental infection.

Ophthalmologists have long known that in human eyes the degree of inflammatory reaction and the incidence of suppurative complications are greater after extracapsular extraction than after the intracapsular operation or any other "clean" intraocular procedure. However, there has not been general agreement as to the factors responsible for this. Discussion of the pertinent literature might be considered under three categories: (1) immunologic reactions with lens; (2) the toxic effects of lens substance; (3) the lens with relation to infection.

The study of immunologic reactions dates from Uhlenhuth's paper[4] showing, by means of precipitin tests, that lens protein was organ specific. This has, in the main, been confirmed by others (Hektoen,[5] Bellows[6]) and has also been demonstrated by anaphylactic reactions (Kodama,[7] Markin and Kyes[8]). The classic paper of Verhoeff and Lemoine[9] on phacoanaphylactic endophthalmitis and the findings of the Johns Hopkins investigators have established it as an entity explaining some of the cases of postoperative inflammation.

The toxic effects of lens substance. Straub[10] developed the concept of phacogenetic endophathalmia, that is, inflammation caused by the presence of lens substance in the ocular fluids. Gifford[11] and de Roetth[12, 13] demonstrated that normal lens substance in the anterior chamber was irritative, that cataractous lens substance was even more toxic, and that nucleus was more toxic than cortex. Injection into the anterior chamber of some of the amino acids present in the lens gave rise to varying degrees of inflammatory reaction. Lens substance was digested by trypsin for a day and the resulting material injected into the anterior chamber. These one-day digests caused no inflammation; two-day digests caused mild iritis; four-day digests, severe iritis.

Braun[14, 15] found that lens substance could bring about contraction of the isolated smooth muscle of the guinea-pig uterus and had a vasodepressor effect not attributed to histamine or acetylcholine. Orlov,[16] by the injection of portions of cataractous lens into the anterior chamber of rabbits, confirmed the greater toxicity of nuclear as compared with cortical material.

The lens as a factor in facilitating infection. This was our major concern in the present investigation. Many of the

*From the Department of Surgery (Division of Ophthalmology), the Department of Medicine, and the A. B. Kuppenheimer Foundation, The University of Chicago. Presented at the 15th scientific meeting of the Association for Research in Ophthalmology, Inc., at San Francisco, July 2, 1946.

standard treatises (Spaeth,[17] Wiener and Alvis,[18] von Blaskovics and Kreiker,[19] de Schweinitz,[20] Meller,[21] Norris and Oliver,[22] Collins and Mayou,[23] and Clapp[24]) make no mention of the relation between lens substance and infection. Czermak and Elschnig,[25] in discussing cataract surgery, advised the removal of the lens remnants and blood clots which form so suitable a medium for the multiplication of introduced bacteria.

De Wecker,[26] in 1883, commented on the greater likelihood of suppuration in operations where the lens capsule was incised than in noncapsulotomizing operations. He did not know why this was so, although he did not think that operative trauma played any important role.

Bacteria, in their effects on the intraocular tissues, were divided by Perles[27] into three large groups: (1) those that multiplied within the eye and caused inflammatory destruction of the organ—that is, panophthalmia; (2) those that did not persist within the eye but before their death caused noticeable inflammation; (3) those that caused no noticeable reaction. Bacteria of the second group, in larger numbers or with increased virulence, could cause panophthalmia; with a decrease in virulence, bacteria of the first group could cause self-limiting changes.

Chibret,[28] in 1888, found that Staphylococcus aureus was not able to survive *in vitro* either in water or in sugar solution, but did grow when lens substance was added. Leber[29] noted perforation of the lens capsule in experimental infection; he attributed this to the action of leucocytes rather than to bacteria or their products.

Andogsky,[30] in 1896, confirmed Chibret's findings and also inoculated the anterior chambers of rabbits with Staphylococcus aureus under various conditions. He found that anterior-chamber inoculation of normal or of iridectomized eyes with small or moderate numbers of organisms resulted in a mild iridocyclitis; inoculation with large numbers of organisms resulted in perforation of the lens capsule and panophthalmia. However, inoculation of capsulotomized eyes with small numbers of organisms caused panophthalmia.

Hancock,[31] in discussing the histopathology of postoperative infection, noted that the process was confined to the anterior segment and that considerable lens matter remained after extraction in the three enucleated bulbs he studied. He was of the opinion that a mild infection was present in most of the cases of severe reaction after extraction.

Treacher Collins[32] demonstrated that lens capsule could heal in the lips of a corneal incision without causing inflammation. He also stated that aqueous humor containing lens substance was a good medium for bacterial growth. In the discussion, Elliot brought up the question of obstruction of the excretory channels by the viscid lens masses as an additional factor.

Lindner[33] called attention to the similarity of lens, skin, and mucous membrane as *epithelia*. He attributed to this the ease with which the pathogenic agents of epithelial tissue caused suppurative inflammation of the eye in the presence of free lens substance. Miklos[34] demonstrated that lens substance was, in general, a better medium for bacterial growth than was aqueous humor, meat extract, or blood serum.

In Velhagen's[35] case of purulent iridocyclitis, in which organisms considered to be gonococci were found in the eye, the lens capsule had ruptured and the organisms were particularly numerous in close proximity to the lens.

In the Lubarsch and Henke handbook, von Szily,[36] under the heading of septic

and experimental traumatic cataract, described in detail the histopathology of septic and aseptic wounds of the lens. Duke-Elder,[37] discussing purulent intraocular inflammations, called attention to the lens because of "the excellent culture medium which its substance provides for the growth of any type of organism."

To summarize the literature: In the first place, the lens has certain special immunologic properties; phacoanaphylactic endophthalmitis is a well-defined clinical and pathologic entity based on these properties. Secondly, the lens has some toxic effects; among its component parts, nucleus is more toxic than cortex, and cataractous nucleus is more toxic than noncataractous. In the third place, there is abundant evidence that lens substance facilitates the multiplication of bacteria. It was toward a clarification of this latter problem with the gonococcus that our work was directed.

Experimental studies

A. In vivo inoculations

Knowing that the lens was in itself toxic to some extent and also that it constituted a favorable medium for bacterial growth in general, we sought to determine what role these factors played in the development of experimental gonorrheal iritis. Several groups of experiments were performed. In one group, a suspension of gonococcus was inoculated into the anterior chamber of the rabbit. In a second group, sterile lens was injected; in a third, a mixture of gonococcus and lens. In a fourth group, gonococcus was inoculated, and the lens simultaneously injured with the hypodermic needle. As a control, in a fifth group, saline solution was injected and the lens injured.

The strain of gonococcus used was one isolated from a sulfathiazole-resistant case of urethritis.* After three passages through the anterior chambers of rabbits' eyes, it was considered suitable for our purposes. Colonies were removed with a loop from the surface of the culture slant and were suspended in physiologic saline solution in a concentration of approximately 100 million organisms per c.c.

Lens substance was prepared in the following manner: The eye of a healthy young adult rabbit was enucleated, and the whole lens removed and placed in a test tube containing 5.0 c.c. of physiologic saline solution. The lens was broken up with a pipette, and the test tube shaken by hand for a few minutes. The resulting suspension had a turbid, opalescent appearance. It was bacteriologically sterile on culture and contained approximately 8 percent of lens substance as calculated from nitrogen determinations by the Kjeldahl method.

Gonococcus-lens mixture was prepared by breaking up a lens in a tube containing 5.0 c.c. of gonococcus suspension.

The volume of injected material was 0.2 c.c. The eyes were observed periodically, and careful descriptions were recorded. These were subsequently reduced, for purposes of tabulation, to symbols indicating the comparative severity of the intraocular reaction. After 8 to 14 days, the rabbits were killed, and cultures were made of the iris and lens.

Tables 1 to 5 summarize the appearance of the eyes and the results of autopsy cultures of the lens and iris. Zero (0) represents a normal eye. Plus-minus ± signifies minimal exudation in the anterior chamber without grossly visible iridic hyperemia. One-plus (+) signifies

* The culture medium used throughout these studies was a casein-digest cystine agar.[1] For the recovery of gonococci from infected eyes, 10-percent fresh defibrinated rabbit blood was added.

TABLE 1

INFLAMMATORY REACTION IN EYES INOCULATED WITH GONOCOCCUS SUSPENSION. LENSES UNINJURED. SERIES 1

Rabbit eye:	1L	2L	3L	4L	5L	6L	7L	8L
Days after inoculation:								
1	±	±	+	+	±	+	+	+
3	±	+	+	+	±	+	+	+
5	0	+	++	+	++	++	±	+
7	0	+	+	±	+	+	±	+
8	0	0	+	0	0	+	0	+
Post-mortem culture of lens and iris:	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

The symbols in this and the following four tables represent the ocular inflammatory reaction as follows: 0=reaction absent; ±=reaction minimal; +=reaction slight; ++=reaction moderate; +++=reaction severe; ++++=reaction maximal.

a moderate amount of exudate in the anterior chamber and slight iridic hyperemia. Two-plus (++) signifies the presence of a small hypopyon, some corneal clouding, and moderate iridic hyperemia. Three-plus (+++) signifies a higher degree of corneal abnormality, a larger hypopyon, and intense iritic changes. Four-plus (++++) eyes generally show an almost opaque and greatly vascularized cornea, through whose more transparent central portions can be seen a hypopyon filling one third to one half of the anterior chamber.

Series 1. Gonococcus suspension was inoculated into eight eyes without injuring their lenses. Five of the eyes became normal in three to eight days; the other three showed one-plus reaction on the eighth day. The average reaction was a little less than one-plus. All post-mortem cultures were negative.

Series 2. Lens substance was injected into eight eyes without injuring their lenses. A maximal reaction of one-plus developed in one eye; the others showed zero to plus-minus reaction. By the fifth day all the eyes were normal. The first four eyes of this group were then used for Series 5.

Series 3. The gonococcus-lens mixture was inoculated into 24 eyes without injuring their lenses. Of the 20 eyes in which the ensuing process developed without complication, 16 had recovered clinically by the day the animals were killed, most of them by the seventh day; of the four eyes which did not, the reaction was one-plus in two, and two-plus and three-plus in one each on the day the animals were killed. The average reaction in these 20 uncomplicated eyes was closer to plus-minus than to one-plus. Of the four eyes in which complications devel-

TABLE 2

INFLAMMATORY REACTION IN EYES INJECTED WITH LENS SUBSTANCE. LENSES UNINJURED. SERIES 2

Rabbit eye:	17L	18L	19L	20L	21L	22L	23L	24L
Days after injection:								
1	±	±	0	±	±	±	±	+
3	±	0	0	0	0	0	0	+
5	0	0	0	0	0	0	0	0
7					0	0	0	0
9	Eyes 17L, 18L, 19L and 20L				0	0	0	0
11	were used for Series 5				0	0	0	0
14					0	0	0	0

TABLE 3

TABLE 3

INFLAMMATORY REACTION IN EYES INOCULATED WITH A MIXTURE OF GONOCOCCUS SUSPENSION AND LENS SUBSTANCE. LENSES UNINJURED. SERIES 3

Rabbit eye:	1R	2R	3R	4R	5R	6R	7R	8R	9R	10R	11R	12R	13R	14R	15R	16R	17R	18R	19R	20R	21R	22R	23R	24R
Days after inoculation:																								
1	++	++	+++++	++	++	+++++	++	+++	+++++	+++	+++++	++	++	++	+++++	+++++	++	++	++	+++++	++	++	++	+++++
3	++	++	+++++	++	++	+++++	++	+++	+++++	+++	+++++	++	++	++	+++++	+++++	++	++	++	+++++	++	++	++	+++++
5	o	o		o	o	++++	+	++	+++++	+++	++++	o	o	+	++++	++++	o	+	o	+++	+	o	o	+
7	o	o		o	o	+++			++++	o	+++	o	o	o	+++	+++	o	o	o	+	o	o	o	+
8						*			++						+	+								
11																								
14																								
Post-mortem culture of lens and iris:	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Gram-neg. bac.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

* 6R—Glaucoma, eye enlarged, A.C. deep.
** 9R—Glaucoma, eye enlarged, A.C. deep.
† 15R—Scleral rupture on first day after inoculation with Gram-negative bacillus as probable secondary invader.
‡ 16R—Glaucoma, eye not enlarged, A.C. deep.

oped, three became glaucomatous, with deep anterior chambers; in two of these, the glaucoma lasted long enough to cause enlargement of the bulbs; in the third, gross enlargement of the bulb did not develop. In the fourth eye of the group with complications, a rupture of the sclera occurred while it was being examined on the day after inoculation. Severe inflammatory reaction developed, and post-mortem culture revealed a gram-negative bacillus. Post-mortem cultures of the other 23 eyes were negative.

Series 4. Gonococcus suspension was inoculated into eight eyes with lens injury at the time of inoculation. These eyes showed, on the whole, a greater inflammatory reaction than those of any other series. When the animals were killed 11 days after inoculation, the reaction ranged from one- to four-plus in five of the eyes. The average reaction during the whole period was between two- and three-plus. The capsular rent in a sixth eye seemed to be healed on the third day, and the reaction had disappeared by the fifth day. The two remaining eyes became glaucomatous, the bulbs enlarging. One of these had an iris bombé; the other a deep anterior chamber. Of the eight eyes, two yielded a heavily positive culture of gonococcus from both the iris and lens.

Series 5. After they had recovered from the previous manipulation, physiologic saline solution was injected, with lens injury, into four eyes from Series 2. Three of the eyes became normal after four days, showing only one-plus reaction. The fourth eye showed persisting one- to two-plus reaction, and post-mortem culture revealed Staphylococcus albus. The other three eyes were sterile on culture.

TABLE 4

INFLAMMATORY REACTION IN EYES INOCULATED WITH GONOCOCCUS SUSPENSION. LENSES INJURED. SERIES 4

Rabbit eye:	9L	10L	11L	12L	13L	14L	15L	16L
Days after inoculation:								
1	+	++	++	+++	++	++++	+	++++
3	+++	+++	++	+++	+++	++++	±	++++
5	+++	+++	++	+++	++	++++	0	+++
7	+++	++	++	+++	++	++++	0	+++
9	++++	++	+++	++	++	++++	0	++++
11	++++	++	++	++	+	+++*	0†	++++‡
Post-mortem culture of lens and iris:	Many gonococci	Neg.	Neg.	Many gonococci	Neg.	Neg.	Neg.	Neg.

* 14L—Glaucoma, eye enlarged, A.C. deep.
† 15L—Capsular tear appeared healed by third day after inoculation.
‡ 16L—Glaucoma, eye enlarged, iris bombé.

TABLE 5

INFLAMMATORY REACTION IN EYES INJECTED WITH PHYSIOLOGIC SALINE SOLUTION. LENSES INJURED. SERIES 5

Rabbit eye:	17L	18L	19L	20L
Days after injection:				
2	+	+	+	+
4	+	±	0	0
6	++	0	0	0
9	+	0	0	0
Post-mortem culture of lens and iris:	Staph. albus	Neg.	Neg.	Neg.

The *in vivo* studies indicated that inoculation of gonococcus together with lens injury was necessary in order to effect a moderately severe inflammatory response. Inoculation, without lens injury, of gonococcus-lens mixture or of gonococcus alone produced only a mild inflammation. Injection of lens substance or aseptic injury to the lens caused a minimal reaction.

B. In vitro studies

In the preceding experiments, about four hours had been required to complete the inoculations. The substances used for inoculation were then cultured to rule out the possibility of bacterial contamination. The cultures indicated that more gonococci had remained viable in the suspension which contained lens than in the one which did not (fig. 1). Studies were accordingly undertaken to determine whether lens substance was able to prolong the life of gonococci in suspension.

Gonococci which had been grown over-

TABLE 6

VIABILITY OF GONOCOCCI IN THE PRESCENCE OF RABBIT LENS

Time:	0	4 hours		1 day		2 days	3 days	4 days	5 days	6 days	7 days	8 days	9days
Dilution:	1:100	1:100	1:10	1:100	1:1	1:10	1:10	1:10	1:10	1:10	1:10	1:10	1:10
Gonococcus (control)	++++	neg.	+++		neg.								
Gonococcus plus fresh lens	++++	++++		++++		++	+	neg. (contaminated)					
Gonococcus plus autolyzed lens	++++	++++		++++		++++	++++	++++	+++	++	+++	+++	neg.

A capillary drop (approximately 0.02 c.c.) was spread out on a culture plate, incubated at 37°C. in a candle jar for 48 hours, and the plates then examined. The following symbols denote the results: neg. = no growth; + = less than 50 colonies of gonococci; ++ = 50–99 colonies; +++ = 100–299 colonies; ++++ = 300–599 colonies; or confluent growth.

night on the surface of a culture slant were suspended in Ringer's solution in a concentration of approximately 100 million microörganisms per c.c. and divided into 3 tubes of 5 c.c. each. One tube served as the control; to the second was added a fresh, macerated rabbit lens; to the third, a rabbit lens which had been macerated and allowed to autolyze in Ringer's solution for 48 hours at 4°C. The number of living gonococci was estimated by culturing serial 10-fold dilutions of each of the tubes. The suspensions were kept at 37°C. and cultures were repeated after 4 hours and 24 hours, and daily thereafter for 9 days.

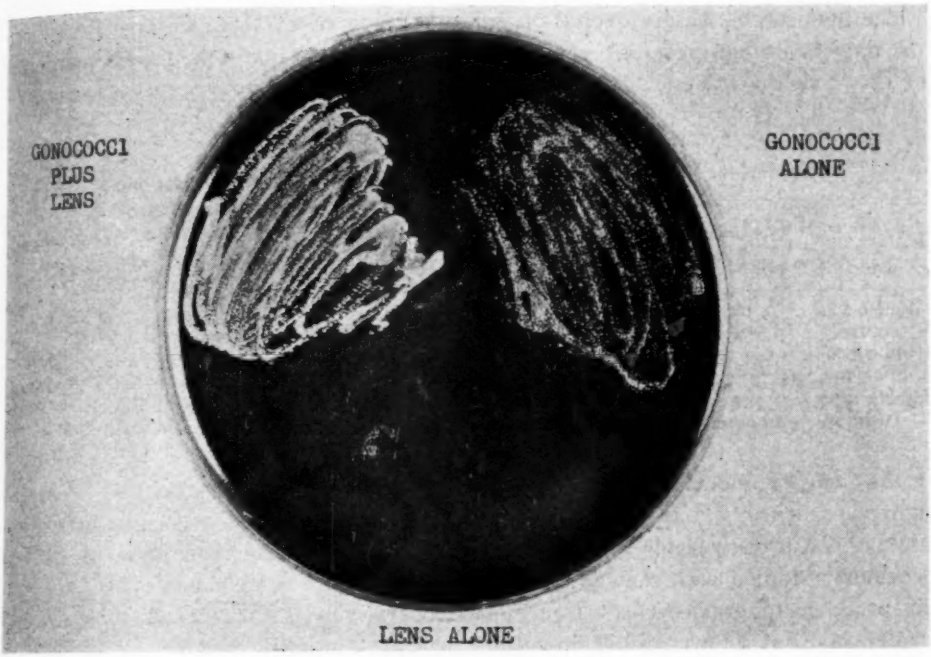


Fig. 1 (Drell, Bohnhoff, and Miller). Culture plate showing greater survival of gonococci in the presence of lens substance than in saline suspension alone. Results of culture of the inoculating materials used in Series 1 to 4.

The results are summarized in table 6. In the control tube, containing no lens, fewer gonococci were viable at four hours and none at one day. In the second tube, containing gonococci and fresh lens, no appreciable change occurred at one day; at two and three days progressively fewer gonococci were viable; at four days, they could no longer be demonstrated on culture. In the third tube, containing gonococci and autolyzed lens, viable organisms persisted for eight days. The cultures were strongly positive for four days and only then began to yield fewer gonococci.

A similar experiment was performed in which a fresh human lens was used. This was a simple senile cataract that had been extracted intracapsularly. The results are summarized in table 7. They were similar to those obtained with fresh rabbit lens. The control tube yielded negative cultures at one day, whereas the tube containing gonococci and lens showed a slight decrease at 24 hours, fewer organisms at two and three days, and none at four days.

Using a variety of solid and liquid media to which both fresh and autolyzed lenses had been added, attempts were made to obtain evidence of *in vitro* multiplication of the gonococcus in the presence of lens, as had been done by Miklos[34] with other microörganisms. These studies yielded negative results.

Comment

The gonococcus was recovered on culture only from that group of eyes (Series 4) in which the lenses had been injured at the time of inoculation. Two of the eight eyes in this group yielded positive cultures. In a comparable group of eyes previously studied with the same strain,[2] the presence of gonococcus was demonstrated in 10 of 12 eyes either on culture or histologic examination. The organism used in the earlier studies had been passed through more than 40 rabbit eyes; it then seemed to be more virulent for the rabbit eye than in the initial stages of animal passage. It should also be pointed out that, in the meantime, the organism had been maintained on artificial media for over a year before the present study was initiated. Since these experiments were designed to compare the effects of gonococci injected under various conditions, three animal passages before use were sufficient.

Andogsky found that injury to the lens at the time of inoculation with Staphylococcus aureus caused panophthalmia. We found that similar inoculation with gonococcus caused only a moderately severe anterior uveitis. The difference is probably due to the less potent pyogenic properties and the more selective cultural requirements of the latter organism.

As a pyogenic agent, the gonococcus occupies a position between groups 1 and 2 of Perles's classification of bacteria in relation to the eye. Ordinarily, a short-term infection results, the microörganism dies, and recovery occurs. Occasionally, however, the gonococcus may be present in great numbers; or it may be so virulent as to cause disruption of the lens capsule (as in Velhagen's case); or postoperatively, sufficient lens substance may be present in the aqueous. Conditions then become favorable, and a severe infection results.

The rapid death of the gonococcus in the eye under ordinary circumstances, with the liberation of its irritative endotoxin, explains the self-limiting and acute nature of ordinary gonorrheal iritis. No allergy nor general toxemia need be postulated. The endotoxin is a poor stimulant of antibody production; this is probably why immunity is so slight and recurrences are so common.

In contrast with most other bacteria, the gonococcus is a fastidious microörganism, requiring certain specific conditions for its survival and multiplication.

TABLE 7

Viability of gonococci in the presence of cataractous human lens

Time	0		1 day				2 days	3 days	4 days
Dilution:	1:1000	1:100	1:1000	1:100	1:10	1:1	1:10	1:10	1:10
Gonococcus (control)	++++	++++				neg.			
Gonococcus plus lens	++++	++++	+	+++	++++		++	+	neg.

Technique and symbols as in table 6.

Our *in vitro* studies indicated that lens, particularly after autolysis, greatly prolonged the organism's survival time. It has been demonstrated by Morax[38] that the survival of the gonococcus without multiplication varies with the individual strain and is in the order of three to nine days. We were unable to demonstrate any multiplication in our *in vitro* studies. McLeod, Wheatley, and Phelon[39] have demonstrated with some of the amino acids a favoring or inhibiting action on growth of the gonococcus. Further studies along this line would be of interest.

Summary

The inoculation of gonococcus into the anterior chamber of the rabbit with lens injury resulted in a moderately severe and chronic inflammation.

The inoculation of gonococcus without lens injury caused a mild inflammatory reaction. Inoculation of gonococcus-lens mixture without lens injury usually caused a similar reaction.

The injection of lens substance without lens injury or the injection of physiologic saline solution with lens injury caused only an insignificant inflammatory response.

Lens substance *in vitro,* particularly after autolysis, prolonged the survival time of gonococci. No clear evidence of multiplication was obtained under these conditions.

630 Medical Arts Building (1).
The University of Chicago (37).

References

[1] Miller, C. P., Drell, M. J., Moeller, V., and Bohnhoff, M. Experimental gonococcal infection of the rabbit's eye. I. Method of production. Jour. Infec. Dis., 1945, v. 77, pp. 193-200.

[2] Drell, M. J., Miller, C. P., Bohnhoff, M., and Moeller, V. Experimental gonococcal infection of the rabbit's eye. II. Course of the disease and its pathology. Jour. Infect. Dis., 1945, v. 77, pp. 201-215.

[3] Miller, C. P., Bohnhoff, M., and Moeller, V. Experimental gonococcal infection of the rabbit's eye. III. Treatment with prophylactic and therapeutic agents. Jour. Infect. Dis., 1945, v. 77, pp. 216-223.

[4] Uhlenhuth. Zur Lehre von der Unterscheidung verschiedener Eiweissarten mit Hilfe spezifischer Sera. Festschrift zum sechzigsten Geburtstage von Robert Koch. Jena, Gustav Fischer, 1903, pp. 49-74.

[5] Hektoen, L. The Specific precipitin reaction of the lens. Jour. Amer. Med. Assoc., 1921, v. 77, pp. 32-33.

[6] Bellows, J. Cataract and anomalies of the lens. St. Louis, C. V. Mosby Co., 1944, p. 197.

[7] Kodama, R. Anaphylaxis produced by eye tissues. Jour. Infect. Dis., 1922, v. 30, pp. 418-432.

[8] Markin, L., and Kyes, P. Species specificity of protein of the optic lens. Jour. Infect. Dis., 1939, v. 65, pp. 156-159.

[9] Verhoeff, F. H., and Lemoine, A. N. Endophthalmitis phacoanaphylactica. Intern. Congr. Ophth., Washington, 1922, pp. 234-284.

[10] Straub, M. Over Ontsekingen van het Oog Veroorzaakt door Oplossing van Lensmassa in de Ooglymphe, Amsterdam, 1919; abstracted in Klin. M. f. Augenh., 1920, v. 65, p. 464.

[11] Gifford, S. R. Allergic and toxic properties of lens protein. II. Toxic properties of lens protein. Jour. Amer. Med. Assoc., 1925, v. 85, pp. 352-356.

[12] de Roetth, A. Experimentelle Untersuchungen über die Bedeutung der Linsenreste für die postoperativen Entzündungen. Ber. d. deutsch. ophth. Gesell., Heidelberg, 1927, pp. 372-377.

[13] ———. Ueber die Bedeutung der Starreste. Arch. f. Ophth., 1929, v. 122, pp. 34-58.

[14] Braun, R. Ueber eine primäre Giftwirkung der Linsensubstanz und ihren Einfluss auf anaphylaktische Experimente. Arch. f. Augenh., 1932, v. 106, pp. 99-144.

[15] ———. Weitere Untersuchungen über die primäre Giftigkeit der Linsensubstanz. Arch. f. Augenh., 1934, v. 108, pp. 341-367.

[16] Orlov, K. Postoperative iridocyclitis after cataract extraction. Sovet. Vestnik Oft., 1935, v. 6, pp. 297-301.

[17] Spaeth, E. B. The principles and practice of ophthalmic surgery. Ed. 3, Philadelphia, Lea and Febiger, 1944.

[18] Wiener, M., and Alvis, B. Y. Surgery of the eye. Philadelphia and London, W. B. Saunders Co., 1940.
[19] von Blaskovics, L., and Kreiker, A. Eingriffe am Auge. Stuttgart, Ferdinand Enke Verlag, 1938.
[20] de Schweinitz, G. E. Diseases of the eye. Ed. 10, Philadelphia and London, W. B. Saunders Co., 1924.
[21] Meller, J. Ophthalmic surgery, edited by W. M. Sweet. Philadelphia, P. Blakiston's Son and Co., 1923.
[22] Norris, W. F., and Oliver, C. A. System of diseases of the eye. Philadelphia and London, J. B. Lippincott Co., 1900.
[23] Collins, E. T., and Mayou, M. S. Pathology and bacteriology of the eye. Philadelphia, P. Blakiston's Son and Co., 1911.
[24] Clapp, C. A. Cataract, its etiology and treatment. Philadelphia, Lea and Febiger, 1934.
[25] Czermak, W. Die augenärztlichen Operationen, edited by A. Elschnig. Ed. 2, Berlin and Vienna, Urban and Schwarzenberg, 1908.
[26] de Wecker, L. In discussion in Bulletins et mémoires de la Société française d'ophthalmologie, 1883, v. 1, pp. 64-65.
[27] Perles, M. Experimentelles zur Lehre von den Infectionskrankheiten des Auges. Virchows Arch. f. path. Anat. u. Physiol. u. f. klin. Med., 1895, v. 140, pp. 209-249.
[28] Chibret, P. Etudes de bactériologie pour la determination d'une antisepsie exacte en ophtalmologie. Avantages de l'oxycyanure de mercure comme antiseptique. Ber. der Intern. Ophth. Congr., Heidelberg, 1888, pp. 385-393.
[29] Leber, T. Die Entstehung der Entzündung. Leipzig, Wilhelm Englemann, 1891, pp. 520-521.
[30] Andogsky, N. Zur Frage über die Infectionsgefahr verschiedener Augenoperationen und über die Bedingungen des Uebergangs der Eiterung aus dem vorderen Theile des Augapfels in die tiefliegenden Augenhäute. Archiv. f. Augenh., 1896, v. 33, pp. 11-34.
[31] Hancock, W. I. Three cases of post-operative infection. Royal London Ophthalmic Hospital Reports, 1912, v. 18, pp. 56-63.
[32] Collins, E. T. In discussion on Post-operative complications of cataract extractions. Trans. Ophth. Soc. United Kingdom, 1914, v. 34, pp. 18-44.
[33] Lindner, K. Ueber die Infektionsgefahr nach bulbusöffnenden Operationen. Zeit. f. Augenh., 1924, v. 53, pp. 305-320.
[34] Miklos, A. Bacterienzüchtung in linsenhaltigen Nährböden. Klin. M. f. Augenh., 1932, v. 89, pp. 481-488.
[35] Velhagen, C. Eitrige Iridocyclitis mit Gonokokken im Augeninnern. Klin. M. f. Augenh., 1937, v. 98, pp. 20-23.
[36] von Szily, A. In Lubarsch, O., and Henke, F.: Handbuch der speziellen pathologischen Anatomie und Histologie. Berlin, Julius Springer, 1937, v. 11 (Eye), part 3, pp. 204-215.
[37] Duke-Elder, W. S. Text-book of ophthalmology. London, Henry Kimpton, 1940, v. 3, pp. 2164-2165.
[38] Morax, V. Apropos de la vitalité du gonocoque. Ann. de l'Inst. Pasteur, 1918, v. 32, pp. 471-475.
[39] McLeod, J. W., Wheatley, B., and Phelon, H .V. On some of the unexplained difficulties met with in cultivating the gonococcus: The part played by the amino acids. Brit. Jour. Exper. Path., 1927, v. 8, pp. 25-37.

Discussion

Dr. S. Judd Beach (Portland, Maine): Dr. James H. Allen asks: "What was the time interval between injection of lens substance in Series 5 and the second inoculation of some of those eyes with injury of the lens in Series 5?"

Dr. M. J. Drell (Seattle, Washington): Five days, by which time the reaction from the injection of lens substance had cleared completely.

Dr. Beach: Dr. M. J. Hogan asks: "Do you think lens substance exerts merely a protective effect on the organisms rather than acting as a culture medium?"

Dr. Drell: That question bothered us for a long time. Dr. Miller has been working with the gonococcus for many years, and the project originally was commenced

at the request of the O. S. R. D., in an effort to produce an experimental infection against which the sulfonamides and other therapeutic agents could be assayed. The gonococcus theoretically ought to grow in the presence of lens. We tried to make it grow but were unable to obtain any clear-cut evidence of its growth. We do know that lens substance is an excellent buffer; the suspension in which lens was present varied only slightly from pH 7.4 to pH 7.2 over a period of five days, whereas the pH of gonococcus suspension alone, in saline or in Ringer's, became acid, dropping from 7.4 to 6.8. This is probably one of the necessary factors. However, the lens also contains a great many of the nutritive agents on which the gonococcus should be able to live and multiply, and we were unable to demonstrate any multiplication.

The survival time of the individual gonococcus has been estimated by Morax to be between three and nine days, varying with the strain. The survival time of gonococcus in our study was eight days. Whether there was any multiplication of any sort during this period we are unable to say positively.

DR. TAUB: Dr. Kinsey wishes to know: "Were culture media tried containing glutathione or other sulfahydrides?"

DR. DRELL: The culture medium used was casein-digest cystine agar prepared in the laboratory. It contained 0.065 percent of cystine, which I do believe is a sulfahydride.

DR. V. EVERETT KINSEY (Boston): Cystine or Cystein?

DR. DRELL: Cystine. This medium was used for the recovery of the organisms from infected eyes. Lens itself contains cystine, which is one of the reasons we thought that the gonococcus would be able to grow upon it.

DR. WALTER B. LANCASTER, chairman, (Boston): Will the essayist tell us whether injury to the lens or other optical injury occurs if the gonococci are introduced intravenously or somewhere outside the eye?

DR. DRELL: I presume the question refers to work similar to that reported by Dr. Rosenau with streptococci. I cannot recall any such investigations with gonococci with any positive results.

Perhaps another word should be added here. The attempt to produce the gonorrheal iritis is nothing new. It has been tried almost since the time that the organism was first described. The organism apparently needs to have its virulence enhanced in some way. The strain used by us was initially enhanced by something like 134 passages through the mouse peritoneum before it was sufficiently virulent for the purposes of producing this iritis.

SPONTANEOUS RUPTURE OF THE LENS CAPSULE IN ANTERIOR LENTICONUS*

LEON H. EHRLICH, M.D.
New York

Spontaneous rupture of the lenticular capsule has been reported as occurring in eight patients to date, in seven instances in association with senile cataracts, some of which had advanced to a morgagnian stage.

Apparently the first mention of this condition was by von Szily,[1] who, in 1884, reported a case of spontaneous rupture of the capsule and, at the same time, mentioned two similar cases by von Ulrich and von Arlt. Some 30 years later, in 1913, Rollet and Genet[2] published a case that occurred in a man, aged 67 years, whose left eye had undergone a successful cataract extraction approximately 12 years previously. The right eye, in which there was a milky (*laiteuse*) cataract, suddenly developed severe pain. Examination revealed a white fluid in the anterior chamber and increased ocular tension. The authors assumed that there had been a rupture of the capsule of the lens.

Gonzales,[3] in 1919, described a woman, aged 75 years, in whose left eye he had noticed a mature cataract 14 years earlier. This eye became painful and, at examination, the anterior chamber was seen to be completely filled with a milky-white liquid. The pressure was much higher than normal.

Kaufman,[4] in 1933, described the case of a man, 58 years old, who had been told 12 years before that he had a cataractous lens in his left eye. When seen, there was a three-day history of pain and redness of that eye. The upper eyelid was swollen. The anterior chamber was filled with a milky-white fluid which hid the details of the iris. Under slitlamp magnification, cholesterol crystals could be seen in this fluid. The intraocular pressure measured 62 mm. Hg (Gradle-Schiøtz).

In 1937, Knapp[5] reported the case of a woman, aged 67 years, with a blind eye, the condition of which had, at one time, been diagnosed as inactive choroiditis. Later, but 23 years prior to the rupture, a mature cataract was noted. Three months before Knapp's examination, one of the patient's relatives noticed an increase in the size of the white spot in the pupil. When seen, there was a mild pericorneal injection and a regularly dilated pupil which was filled with a white mass extending into the anterior chamber. The tension was recorded as 42 mm. Hg (Schiøtz).

The most recent case was reported by Box[6] in 1941. His patient was the youngest to be reported with this condition. Since the age of 18 years, he was known to have opacities of both lenses which were thought to be congenital; their extent was not described. At the age of 34 years, an immature cataract reduced the vision of the left eye to perception of hand movements, with good light projection. About two years later, the patient returned with a history of improved vision in the left eye and deterioration of vision in the right. An iridocyclitis which the author regarded as of tuberculous origin was found in the right eye. The left eye appeared aphakic despite the absence of a history of trauma or surgery. X-ray examination showed no evidence of a foreign body. No corneal scar could be seen. Examination under the slitlamp revealed a temporal gap in the anterior lens capsule and some soft lens matter still present. After a needling op-

* From the ophthalmological service of Beth Israel Hospital.

eration was performed for the latter condition, corrected vision ultimately was 6/6 partly.

For completeness, another case may be added to this list. However, the element of trauma makes its inclusion in this series controversial. Beisbarth[7] performed an iridectomy for secondary glaucoma on the eye of a woman, aged 65 years. Tension fluctuated between 25 and 37 mm. Hg (Schiøtz), and there was an increased cloudiness of the lens. The eye seemed to tolerate the operation but five weeks later it became painful and, during the night, the patient experienced excruciating pain. In the morning, she said something had come out of the eye and brought to the ophthalmologist, as proof, a lens nucleus on a piece of gauze. Examination showed a small round hole at the limbus through which a tag of capsule appeared.

Anterior lenticonus

Cases of anterior lenticonus are more frequent than rupture of the lens capsule. Only the literature on this subject that has appeared since the publication in 1934 of the paper by Rones[8] will be mentioned here. He listed 10 recorded cases in which the diagnosis of anterior lenticonus appeared justified. In addition, he mentioned several other cases which he considered incorrectly diagnosed as lenticonus. Since then, a search has revealed 10 additional cases.

In 1936, Moulton[9] described the case of a man, aged 33 years, who had bilateral lenticonus. Biomicroscopic examination showed that in each eye the anterior band of the lens and the anterior band of disjunction curved forward over the clear underlying contents of the conus. There was no alteration in their parallelism nor change in their thickness. The nucleus and posterior cortex of each lens were normal. A very few minute, delicate opacities were visible on the apex of the cones and just beneath the intact anterior capsules.

Rauh,[10] in 1936, reported the case of a man, aged 48 years, who had a lenticonus of each eye in which only the zone between the adult nucleus and the capsule bulged forward. The nucleus itself appeared normal in contour in each eye.

Knobloch[11] described, in 1937, anterior lenticonus developing in both eyes of a motion-picture operator, aged 20 years. According to an abstract, which was the only report available to the author, slit-lamp examination showed arching of the anterior capsule only, but not the limits of the surface between the detached zone and the cortical zone.

In 1939, Zavalia and Oliva[12] described the cases of two brothers, aged 23 and 15 years, in whom uncomplicated anterior lenticonus developed at puberty. The parents were cousins. This consanguinity and the presence of lenticonus in the siblings emphasized the role of heredity in this report, although apparently it played no obvious part in any of the cases described elsewhere. The older brother had lenticonus in both eyes. The condition was unilateral in the younger brother, but the fellow eye had an anterior-central capsular cataract. The illustration of the lenticonus in the younger patient showed an asymmetry in the protrusion of the anterior capsule and its underlying cortex which was not present in the regular curve of his brother's lenticonus. In this latter patient, there was seen a concavity in the usual convex surface of the anterior band of the adult nucleus corresponding to the lenticonus.

Ter-Artuniantz, Kotilianskaja, and Chutko[13] reported, in 1939, two cases with all the symptoms of posterior lenticonus, but subsequently biomicroscopy demonstrated that one of these was a case of anterior lenticonus.

In 1940, Harris[14] described the case of

a man who, for as long as he could recall, had had poor vision and was forced to leave school at the age of 16 because his sight suddenly and rapidly deteriorated. Slitlamp examination showed, in each eye, a globular protrusion of the anterior cortex and capsule through the pupil to within 0.5 mm. of the cornea. The anterior cortex and the capsule of each lens alone were implicated in the lenticonus. The nuclei were of normal configuration. However, just behind the center of the nucleus, were discoid punctate cataracts which were round and finely granular.

In 1942, Damel and Garbarino[15] reported the case of a man, aged 24 years, whose vision had become poor when he was 15. He had bilateral lenticonus. The lens capsule and the anterior cortex presented the usual forward bulge, with a normal underlying nucleus.

Rocha and Coscarelli[16] described, in 1943, a 30-year-old woman with bilateral lenticonus, the base of each cone being about 3 to 4 mm. in diameter. There were a few opacities of the coronary type, as well as some filaments of persistent pupillary membranes between the lens and the iris.

Marback[17] published the most recent report in 1943. His case, occurring in a man aged 23 years, was one of microphakia with a lenticonus on the anterior face of each lens. The deformity involved the anterior capsule and the anterior half of the senile nucleus, the fetal nucleus appearing normal. The condition of the cortex was not described.

Case report

L. S., a boy, aged 12 years, was first seen on May 20, 1944, with a history of having worn spectacles for two years. He first realized that he had a defect of vision three years before, when his right eye became red after a mild blow received during a fist fight with another youngster. There was a history of nephritis, hay fever, and asthma. Urinalysis showed the presence of albumin 2+, red blood cells, and casts. There was no edema. The blood pressure was 120/70.

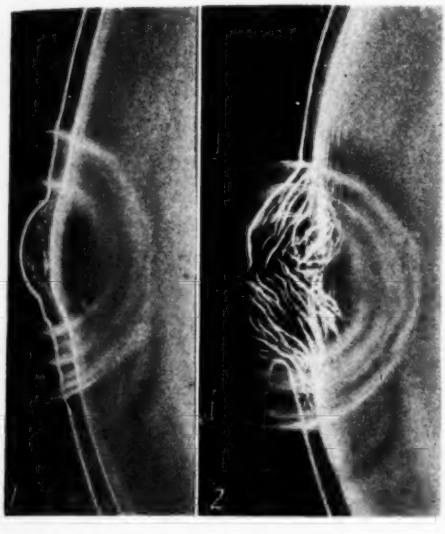
Vision of the right eye was 4/200 and could not be improved. Retinoscopy revealed the characteristic appearance of a droplet of oil in the retinal reflex. The external and ophthalmoscopic examination presented no abnormalities. On examination with the slitlamp, there was seen a bulging forward of the anterior capsule in the axial region. The diameter of the bulge appeared to be 2.5 mm., and the elevation possibly one fourth the depth of the anterior chamber. This elevation seemed filled with a clear liquid which separated the anterior capsule from the lens substance. There was a very small amount of pigment on the capsule at the base of the elevated area (fig. 1).

The left eye appeared normal on external, ophthalmoscopic, and slitlamp examination. The reflex on retinoscopy was normal. There were 2.25 diopters of hypermetropia. Corrected vision was 20/20.

The patient was next seen a month later. At this time, the father said he had noticed, about a week and half previously, that there was a white substance in the pupillary region of the right eye. There had been no previous injury of any kind to either the eye or the head. Visual acuity was found to be reduced to the perception of hand movements. Soft lens material obviously protruded into the anterior chamber. Under the slitlamp, a tear could be discerned in the anterior lens capsule at the summit of the elevation. Swollen cortex presented through the tear into the anterior chamber (fig. 2). The intraocular pressure in each eye was 15 mm. Hg (Schiøtz). Atropine was prescribed. It was decided to keep the eye under observation.

When seen three weeks later, the boy said that he had struck the right eye two days before. At this examination some of

the lens material was observed to have broken loose from the main mass, which was now larger than before, and was present in the lower part of the anterior chamber, descending almost to the angle. A few weeks later this separated lens substance had become absorbed. The area of opacification extended beyond the limits of the elevation of the capsule and spread about halfway to the equator of the lens. By November, the lens was almost entirely cataractous. An exotropia of about 20° was present. On January 26, 1945, a linear extraction of the cataract was performed, and the greater part of the lens washed out. Because of persistent prolapse of the iris, a narrow iridectomy was made. A month later, vision of the right eye was 20/20 with a +12D. sph. ⌒ +1D. cyl. ax. 180°.



Figs. 1, 2 (Ehrlich). Slitlamp appearance of eye with anterior lenticonus. Fig. 1. Showing pigment at base of elevation. Fig. 2. Ruptured capsule.

While all this was taking place, changes began to be evident in the left eye. In September, 1944, a minute dot was seen in the anterior capsule. In the course of three months, two dots with a connecting line between, in a sort of dumbbell arrangement, could be made out under the slitlamp. After a year of progress, this gray area on the lens capsule showed considerable enlargement and seemed to have the form of a horseshoe (fig. 3).

Fig. 3 (Ehrlich). External appearance a year later.

Discussion

Spontaneous rupture of the lens capsule obviously will take place when the volume of the lens is greater than can be contained within the elastic capsule which, however, may stretch in compensation. Modifying factors will be: (1) Rapidity of the swelling; (2) variations of capsular tensile and elastic factors; (3) location of the swelling when not diffuse but confined to a portion of the lens.

That there is elasticity of the lens capsule to permit swelling was observed by Bowman[18] who stated: "When removed from the eye and placed in water, the lens imbibes fluid through its capsule, which thereby becomes distended and separated from the contained lens, being raised in the form of a vesicle." Limitations naturally exist as to the amount of capsular stretching that can take place under such conditions, as has been shown by Bellows

and Chinn,[19] who reported the spontaneous bursting of some lenses by swelling when subjected to various chemical solutions and altered physical conditions. One would assume that slow swelling, taking place over long intervals, would permit of greater volume without rupture of the lens capsule. This, however, can only be surmised. It is obvious that there is some limit to the extent of capsular enlargement.

The capsule increases in thickness with age. Whether this adds to or diminishes its tensile capacity cannot be stated. It is, perhaps, related to the diminution of its permeability with age as Friedenwald[20] has demonstrated.

Another theoretical consideration revolves about the possibility of the capsule sliding over the surface of the lens. If a small, localized elevation occurs anywhere on the lens surface, the overlying capsule will be subject to less strain if the entire capsule, or at least a large portion of it, shifts its position toward the region of the swelling. Otherwise, it is the portion of capsule immediately overlying the swelling that must bear the entire burden of adaptation to the new conditions, with a consequent increase in the possibility of rupture. When liquefaction of the lens substance occurs, increased pressure is distributed uniformly throughout the lens.

Alteration in the strength of the capsule undoubtedly accurs in the pathologic condition represented by morgagnian cataract. Duke-Elder[21] apparently attributes to this factor the known cases of spontaneous rupture herein listed as well as the hypothecated ones wherein rupture is considered as being the possible explanation for some of the reported cases of spontaneous absorption of a morgagnian cataract, stating that they may be due to a rupture "in the thin capsular wall." Kaufman[4] also has observed that the wall of the capsule is always thin in these cases. Under these conditions of weakening of the capsule, a sudden increase in the intralenticular pressure or an alteration in relationship between the intralenticular and intraocular pressures could easily be the immediate and exciting factor in the rupture of the lens capsule. Ordinary daily activities and stresses or a sudden imbibition of fluid resulting from altered osmotic pressure relationships (possibly a result of disintegration of the lens protein) could increase or alter these pressures.

Senile and morgagnian cataract need not be the only varieties to provide the conditions for spontaneous rupture. Box's[6] case occurred in the eye of a 36-year-old man, although it is possible that the morgagnian type of disintegration of the lens substance took place in the 27-month interval between the time when he was observed to have an immature cataract and when he returned manifesting a gap in the capsule of the partly absorbed lens.

Another case, more closely resembling the one here reported, is that of Feigenbaum.[22] The patient was an Arabian youth with bilateral anterior lenticonus who, over a period of three years, had shown an increase in the lenticonus. When seen again, after another three-year interval, the right eye was essentially unchanged. Retinoscopy, however, revealed only a slight myopic astigmatism of the left eye in place of the 9 diopters of myopia previously present in the central portion of the lens. At this time, the patient said he had noticed a corresponding improvement in his vision. Biomicroscopy showed the protrusion to have been replaced by a somewhat dense subcapsular opacity at the same spot and of about the same size as the former lenticonus. Feigenbaum concluded that the increase in the convexity at the anterior pole "caused the capsule to burst in one place, resulting in a localized opacity, which means that a self-healing of the lenticonus

took place." Such a change from anterior lenticonus to anterior capsular cataract has also been described by Jaworski[23] and Tsukahara,[24] and both were attributed to a similar pathogenesis by Feigenbaum.

Jaworski's case was that of a 32-year-old man who had a bilateral lenticonus. When seen eight months later, there was present in the right lens a 2-mm. opacity in place of the lenticonus. In the left lens, there was a similar opacity, but a small amount of protrusion could still be made out. Unfortunately, this case was reported in the days before the slitlamp came into use, and so small capsular ruptures could easily be overlooked.

Rones[8] believed that Tsukahara's second case does not properly belong with those called lenticonus, but it may well have been because the original article was published in Japanese, and the abstract in German does not give sufficient details to eliminate it definitively from this category. Tsukahara's first case obviously should not be included. His second case was of a 17-year-old boy with a unilateral lenticonus. Eight months later an anterior capsular cataract was added to this lenticonus. At this time the previously normal lens of the left eye also had an anterior capsular cataract. It is difficult to understand, on the basis of this meager information, how Feigenbaum can postulate a rupture in the lens capsule.

Review of the reported cases reveals two significant features: In every instance both eyes were sooner or later involved. This, in most instances, took the form of lenticonus in each eye. The exceptions are the younger of Zavalia and Oliva's two brothers, who had an anterior capsular cataract in one eye and lentiglobus in the other; the case of Tsukahara just described; and Feigenbaum's case after the disappearance of the lenticonus in the left eye.

The other feature is that the pathologic process in almost every case involved the anterior capsule and cortex only. Of course, cases reported prior to biomicroscopy cannot be included. Exceptions to the localization of the pathologic process were: (1) the older of the two brothers described by Zavalia and Oliva who had a concavity in the normal uniform convex curve of the anterior band of the adult nucleus. (2) Harris's[14] case presented, in addition to the lenticonus which involved only the anterior capsule and cortex, discoid punctate cataracts just behind the center of the nucleus. (3) Marback[17] states that the deformity in his patient lay in the anterior capsule and the anterior half of the senile nucleus, the fetal nucleus being normal.

Ter-Artuniantz, Kotilianskaja, and Chutko's case[13] is not included in the generalizations just made regarding bilaterality and the lack of nuclear involvement because the original article was not available and the abstract did not describe these features.

Any theory as to the origin of anterior lenticonus must account for the normal appearance of the nucleus. It is difficult to comprehend how a congenital disturbance would permit the nucleus to develop normally and make its effect felt only after puberty. The bilaterality of the lesion and the lack of a hereditary tendency (only Zavalia and Oliva's brothers present such a factor) would point to a metabolic disturbance. The nephritis of the patients of Kienecker[25] and Jaworski[23] and the two constitutional elements of allergy and nephritis in the case here reported give some support to such an element in the causation of anterior lenticonus. In their articles, Rones[8] and Bellows[26] both discuss the various theories of the causation of anterior lenticonus, which need not be repeated in this report.

Although the accuracy of the diagnosis of anterior lenticonus in the case herein described may well be questioned, there

seems to be no other described condition that corresponds to it more closely. Vogt's atlas,[27] as well as the smaller one of Meesmann,[28] illustrates no similar case, nor is one included in Bellow's recent encyclopedic work on cataract and lenticular anomalies.[26] The process in the right eye seems similar to the one Feigenbaum[22] described as occurring in the left eye of his patient except that the rupture in the latter case must have been much smaller. If the anterior capsular change of the lens of the left eye which developed during the period of observation had been present when the patient was first seen, it would have appeared essentially the same as that of the younger of Zavalia and Oliva's patients. In Tsukahara's case, the anterior capsular cataract also developed during observation. The spontaneous improvement in both eyes of Jaworski's patient, within an interval of only eight months, indicates the rapidity with which such a change may occur. Our patient was seen only by chance in the interval between the breakdown and liquefaction of the lens substance in the lenticonus, when rupture of the extended and strained capsule was imminent and before the actual rupture of the membrane took place.

Summary

A case of anterior lenticonus in a boy is described. It is unusual in that it was unilateral; that the cone contained liquefied lens material; and that it ruptured spontaneously. During the period of observation, the left eye developed central-anterior capsular changes.

The literature on spontaneous rupture of the lens capsule and on anterior lenticonus has been summarized and discussed in relation to the case here reported.

211 Central Park West (24).

References

[1] Szily, A. v. Cited by Kaufman.[4]
[2] Rollet and Genet. Cataracte laiteuse ouverte spontanement dans la chambre antérieure. Rev. Gen. d'Opht., 1913, v. 32, p. 1.
[3] Gonzalez, J. de J. Spontaneous rupture of morgagnian cataract. Amer. Jour. Ophth., 1919, v. 2, p. 742.
[4] Kaufman, S. I. Morgagnian cataracts and their complications. Arch. of Ophth., 1933, v. 9, p. 56.
[5] Knapp, H. C. Spontaneous rupture of the lens capsule causing secondary glaucoma. Amer. Jour. Ophth., 1937, v. 20, p. 820.
[6] Box, W. M. Spontaneous absorbtion of cataract. Med. Jour. Australia, 1941, v. 28, p. 451.
[7] Beisbarth, C. Spontaneous expulsion of cataract nucleus. Amer. Jour. Ophth., 1937, v. 20, p. 184.
[8] Rones, Benjamin. Anterior lenticonus. Jour. Amer. Med. Assoc., 1934, v. 103, p. 327.
[9] Moulton, E. C. Anterior lenticonus. Jour. Amer. Med. Assoc., 1936, v. 107, p. 1809.
[10] Rauh, W. Anterior lentiglobus. Zeit. f. Augenh., 1936, v. 89, p. 321.
[11] Knobloch, R. Abstracted, Amer. Jour. Ophth., 1938, v. 21, p. 476.
[12] Zavalia, A. V. and Oliva, A. O. Consideraciones sobre dos cases de lentiglobo anterior. Arch. de Oft. de Buenos Aires, 1939, v. 14, p. 848.
[13] Ter-Artuniantz, C. M., Kotilianskaja, P. I., and Chutko, M. B. (Abstr.) Amer. Jour. Ophth., 1940, v. 23, p. 959.
[14] Harris, C. F. Bilateral anterior lenticonus. Northwest Med., 1940, v. 39, p. 219.
[15] Damel, C. S. and Garbarino, A. Lenticono anterior. Arch. de Oft. de Buenos Aires, 1942, v. 17, p. 363.
[16] Rocha, H., and Coscarelli, E. Lenticone anterior. Ophthalmos, 1943, v. 3, p. 219.
[17] Marback, H. Sinal da gota de oleo na pupila microfaquia-lenticone anterior. Arquivos Brasileiros de Oft., 1943, v. 6, p. 119.
[18] Bowman, W. Cited by Bellows,[26] p. 132.
[19] Bellows, J. G., and Chinn, H. Biochemistry of the lens. 15 studies on the swelling of the isolated lens. Amer. Jour. Ophth., 1941, v. 24, p. 979.

[29] Friedenwald, J. S. The permeability of the lens capsule to water, dextrose and other sugars. Arch. of Ophth., 1930, v. 4, p. 350.
[30] Duke-Elder, W. S. Text-book of ophthalmology. St. Louis, C. V. Mosby Co., 1941, v. 3, p. 3171.
[31] Feigenbaum, A. Origin of lenticonus anterior. Folia Ophth. Orient., 1932, v. 1, p. 103.
[32] Jaworski, A. Ein Fall von Lenticonus anterior und über dessen Entstehen. Arch. f. Augenh., 1910, v. 65, p. 313.
[33] Tsukahara. Acta Soc. Ophth. Japan, 1930. Abstracted in Zentr. f. ges. Ophth., 1931, v. 24, p. 171.
[34] Kienecker, R. Ueber einen Fall von doppelseitigem sog. Lentiglobus anterior. Klin. M. f. Augenh., 1929, v. 82, p. 55.
[35] Bellows, J. G. Cataract and anomalies of the lens. St. Louis, C. V. Mosby Co., 1944.
[36] Vogt, A. Lehrbuch und Atlas der Spaltlampen mikroskopie Auges. Berlin, J. Springer, v. 2.
[37] Meesmann, A. Die Mikroskopie des lebenden Auges an der Gullstrandschen Spaltlampe mit Atlas typischer Befunde. Berlin, Wien, Urban & Schwarzenberg, 1927.

CONTUSION CATARACT OF THE ANTERIOR LENS CAPSULE*

HERBERT F. SUDRANSKI, M.D.
Indianapolis, Indiana

The traumatic cataract described by Vossius[1] is thought to originate from the deposit of uveal or blood[2, 3] pigment upon the anterior lens capsule at the pupillary margin when the iris is forced against the lens by contusion of the globe. A recent case of perforating injury of the eye presented a cataract of similar etiology. This cataract involved the anterior lens capsule only. A perfect, although very faint, imprint of the circular sphincter pupillae muscle fibers and of the radial markings of the iris was stamped upon the anterior lens capsule. It contained no pigment, and was a much more complete reproduction of the iris anatomy than the pigmented ring or arc which marks the site of the pupillary margin upon the anterior lens capsule in cases of Vossius-ring cataract. This lenticular opacity appears to be a unique variety of traumatic cataract not yet reported in the ophthalmic literature.

CASE REPORT

History. D. M. D., an aviation machinist mate, aged 20 years, was examined on August 2, 1945, to determine his fitness for sea duty. His medical record confirmed a remarkable history of trauma to his right eye. On December 3, 1944, while he was engaged in cleaning a metal lathe with a medium-pressure air line (50 lb.), he was struck in his right eye by a blast of air when, for a moment, he lost control of the hose. Two days later he reported to his sick bay, complaining of pain and redness of his right eye. Corneal ulceration was noted at the 8-o'clock position, with cloudiness of the cornea below. Ophthalmoscopy revealed a triangular, metallic foreign body lying within the vitreous in the lower temporal aspect of the fundus. Roentgen examination showed two metallic foreign bodies, in the lateral view, in line with the orbits. These were not visualized in the posterior-anterior view.

At the United States Naval Hospital, in Oakland, California, it was noted that the patient had a healed, perforating wound of the cornea at the 9-o'clock position. Beneath this wound, the iris was

*From United States Naval Hospital, Astoria, Oregon. The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service.

punctured, and there was a visible track through the lens. Six disc diameters along the inferior temporal vessels, a shiny foreign body, measuring one disc diameter in length and one-fifth disc diameter in width, was visible upon ophthalmoscopy and appeared to be located 1 mm. from the retina. Roentgen studies failed to show any foreign body in or near the right eye. Conservative treatment, consisting of the instillation of atropine and application of heat locally, was followed. By January 2, 1945, the right eye was free of pain and all visible signs of inflammation. After 30 days, there having been no appreciable change in the condition of the right eye, the patient was returned to duty.

Examination. When this patient was examined in August, 1945, bilateral vision was 20/15. The left eye, upon external examination, palpation of the intraocular pressure, and ophthalmoscopy, was entirely normal. The right eye showed a penetrating scar of the cornea located at the 9-o'clock position, 2.0 mm. within the limbus. It was 0.5 mm. in width and 2.0 mm. in length, being directed obliquely upward toward the corneal vertex. Slightly above the corneal wound and just within the limbus, there was a faintly atrophic scar of the iris which measured 1.0 mm. in width and extended vertically 2.0 mm. No track could be located within the lens. The ocular tension to palpation was normal. By focal illumination and by biomicroscopic examination with diffuse direct illumination, a complete reproduction of the circular sphincter pupillae muscle fibers and of the radial pattern of the iris was observed to have been laid down upon the anterior lens capsule, in faint, grayish-white markings. These markings were confined to the lens capsule and contained no pigment. The biomicroscope showed no other lenticular pathologic change, but revealed a finely granular disorganization of the vitreous in the zone immediately behind the lens. Ophthalmoscopy showed no pathologic lesion in the ocular media other than the corneal scar. The cataractous changes of the anterior lens capsule and the vitreous disorganization were invisible. The fundus was essentially normal, although its lower temporal region showed very slight disturbance of the retinal pigment. No trace could be found of the previously reported metallic foreign body.

Roentgen report. The Hospital roentgenologist made the following report: "There are two minute, opaque foreign bodies in the region of the right orbit. The first measures approximately 1.0 x 1.0 x 0.25 mm. It is extraocular in location. The second measures approximately 1.0 x 0.5 x 0.25 mm. It lies 11.5 mm. below the horizontal plane of the cornea, 4 mm. to the temporal side of the verticle plane of the cornea, and 13 mm. behind the center of the cornea; therefore, it lies in or close to the sclera."

Discussion

This case has several features of unusual interest. It would appear that the retained metallic foreign body was either completely absorbed or that it was extruded from the eye by migration through the sclera. The absorption of foreign particles within the eye (for copper) was first reported by Leber[4] in 1892. Fifty years earlier Castelnau[5] had reported the migration of intraocular foreign bodies through the sclera. Extrusion of such a particle, according to Cordes and Harrington,[6] is accompanied by ocular inflammation with softening of the sclera. Since, in this case, all inflammatory reaction had subsided within the 30th day after the accident, the foreign body remaining visible to ophthalmoscopic examination all the while, it would appear that transcleral migration

had not occurred. However, after the accident, two metallic foreign particles were visualized by X-ray examination. Again, when this patient presented himself for examination for fitness for sea duty, seven months later, two metallic foreign bodies (one of which was localized in or close to the sclera) were still demonstrable by the X ray. Two observations would appear to afford sufficient evidence that, in this case, the intraocular metallic foreign particle may have been actually extruded from the eyeball by transcleral migration; namely, (1) the foreign bodies roentgenographically visible were not reduced in number (even though the one at first observed within the vitreous had later disappeared), and (2) the slight disturbance of the retinal pigment in the lower temporal portion of the fundus.

Even more remarkable is the presence of grayish-white opacities of the anterior lens capsule so arranged as to reproduce, in detail, the anatomic markings of the posterior iris surface. This finding may be regarded as typical of a distinct category of traumatic cataract not previously described. Impact of the iris against the lens, due to the application of tremendous force to the eyeball, has effected permanent alteration of the tissue of the anterior lens capsule. This alteration of the lens-capsule tissue is evidenced by loss of transparency; it is intrinsic and not related to the deposition of uveal or blood pigment as is the case in instances of Vossius-ring cataract. The contusion cataract of the anterior lens capsule is illustrated photographically in figure 1.

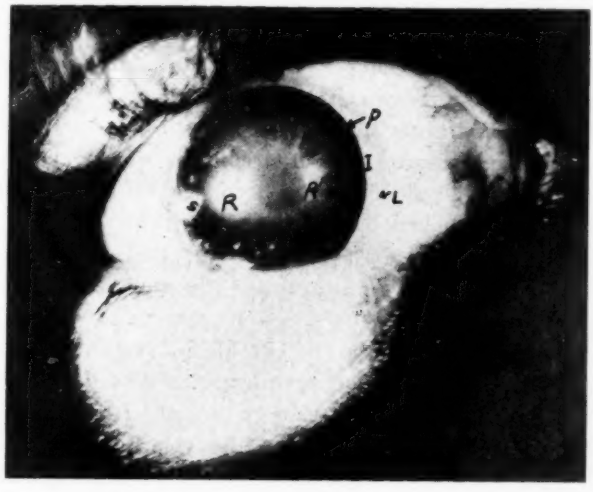


Fig. 1 (Sudranski). Photograph of the right eye, made under intense focal illumination (directed from the temporal side) with the pupil widely dilated, showing the pupillary margin at P, the corneal limbus at L, and the folded iris tissue at I. S marks the site of the scar near the corneal limbus temporally and directed toward the corneal vertex. The large, bright reflex from the anterior surface of the cornea is at R. The smaller, fainter reflex from the anterior surface of the lens is at R′. The latter is seen at the same level as the cataractous markings of the anterior lens capsule, C. The far periphery of the lens appears entirely black, indicating that the anterior lens capsule is uninvolved where the lens surface, near its equator, curves sharply away from the plane of the iris. (Official U. S. Navy photograph.)

Although the iris, at its free margin, lies practically in contact with the anterior surface of the lens, yet there is a thin layer of aqueous intervening. Therefore, pressure directed upon the anterior aspect of the eyeball, however great and however sudden in origin, must, according to the laws of physics, be distributed equally throughout the globe. Because of the free communication of the anterior and posterior chambers through the pupil, it should not be possible for any pressure change within the eye to force the iris

against the lens, for the equal distribution of pressure throughout the globe would result in as great a pressure being exerted away from the lens from the posterior chamber as toward it from the anterior chamber. However, this conception of the ocular hydrodynamics fails to consider the fact that the eyeball is a structure of living tissues whose physiologic activity considerably modifies the operation of purely physical laws. In the closed space of the living eyeball, the intraocular pressure is maintained by the circulation of blood through the vascular system, the secretion of aqueous by the ciliary body (in turn dependent upon the circulation), and the drainage of aqueous through Schlemm's canal and the venous system. Sudden pressure upon the eyeball, by increasing the intraocular pressure, cuts off the arterial circulation, reduces the secretion of aqueous by the ciliary body, and forces the exit of aqueous through the drainage channels. As the aqueous drains from the anterior chamber, it is replaced by fluid from the posterior chamber which, due to slowing of the circulation through the ciliary body, is not renewed. Therefore, the iris may be forced against the lens in all or part of its pupillary circumference. In this fashion, the ring cataract of Vossius may originate. However, the physiologic modification of physical hydrodynamics within the eye would hardly appear to be adequate to account for the forceful application of the entire posterior iris surface against the anterior surface of the lens.

To provide physical conditions that would make such a movement of the iris possible, the force producing a pressure change would have to become operative after the escape of fluid from the eye had been effected. With rupture of the eyeball, the continued application of pressure would cause the aqueous to be forced from the anterior chamber through the wound. At the same time, movement of the aqueous through the pupil into the anterior chamber would empty the posterior chamber of fluid. With the emptying of the posterior chamber, continuing pressure would then force the iris against the anterior surface of the lens at the same time draining aqueous from the anterior chamber until, if the pressure-producing force acted for a sufficiently long period of time, the cornea would eventually be applied to the anterior surface of the iris.

In the case here reported, conditions would appear to have been ideal for driving the entire iris against the lens. Rupture of the globe was accomplished by metallic particles driven through the cornea by a blast of air under pressure. How ideal these conditions were is obvious if it is assumed that the metallic particles struck the eye with the initial current of compressed air which then continued its force until turned away by the patient. Only a very short period of time was needed for such a force to empty the aqueous from the posterior chamber and drive the iris against the anterior surface of the lens. Absence of even the slightest macular damage is strong evidence favoring this theory, for it is reasonable to suppose that the force of a 50-pound stream of compressed air would surely have damaged the macula by contrecoup if the globe had not been opened at the very instant of the blast.

Contusion cataract of the anterior lens capsule, therefore, appears to originate in trauma which exerts a force continuing for a period of time after it has effected rupture of the globe. Circumstances which produce trauma of this type must be of most infrequent occurrence. Hence this variety of traumatic cataract should be a great rarity.

23 East Ohio Street (4).

References

[1] Vossius, A. Ring-shaped opacities on the anterior surface of the lens after contusions of the eye. Arch. of Ophth., 1906, v. 35, pp. 566-567.
[2] Hesse, R. Zur Genese der Vossiusschen Ringtrübung. Zeit. f. Augenh., 1919, v. 41, pp. 226-228.
[3] Zentmayer, William. The pathogenesis of Vossius ring cataract. Amer. Jour. Ophth., 1924, v. 7, pp. 676-677.
[4] Leber, Theodor. Trans. Ophth. Soc. United Kingdom, 1892, v. 12, p. 4.
[5] Castelnau, R. Expulsion of intraocular foreign bodies. Arch. of Gen. Med., 1842, v. 15, p. 210.
[6] Cordes, F. C., and Harrington, D. O. Bilateral absorption of intraocular copper with chalcosis in one eye. Amer. Jour. Ophth., 1935, v. 18, p. 4.

A STATISTICAL REVIEW OF 367 BLINDED SERVICE MEN, WORLD WAR II

FREDERIC H. THORNE, COL. (MC), U.S.A. (*Retired*)
San Antonio, Texas

The following statistics were compiled from the first 367 consecutive admissions of blinded service men of the Army to Old Farms Convalescent Hospital (Special), Avon, Connecticut. If all the World War II blinded, of which there will be approximately 1,000, were included in this review, some variations would be noted in the distribution, causes, and so forth, particularly in those cases due to disease. However, it is felt that this number of consecutive admissions will present quite an accurate picture of those blinded in the present war.

Early in World War II, two Army general hospitals were designated as centers for the medical and surgical care of the Army blinded. These hospitals were Valley Forge General Hospital, Phoenixville, Pennsylvania, and Letterman General Hospital, San Francisco, California. The blinded activity at Letterman General Hospital was transferred to Dibble General Hospital, Menlo Park, California, upon activation of the latter in 1944, while Valley Forge General Hospital continues to operate as a center for the blinded. At these two centers, concurrent with medical and surgical treatment, the blinded are given preliminary social-adjustment training consisting of Braille reading, typing, orientation, occupational therapy, and related subjects. Upon completion of hospital treatment, the blinded are transferred to the advanced social-adjustment training center for the blinded at Old Farms Convalescent Hospital (Special), Avon, Connecticut, which was activated June 14, 1944.

The advanced social-adjustment training consists of a continuation of the adjustment begun in the two blinded centers referred to, and, in addition, there are available approximately 50 subjects and try-out jobs from which the trainee may select as many as he desires or is capable of pursuing. Among these are wood working, machine-shop work, factory jobs, counseling, guidance, business management, vending-stand operation, agriculture, book-binding, music, and similar occupations. Upon completion of advanced social adjustment, which requires approximately 18 weeks, the blinded man is discharged from the service and returned to his home.

Definition of Blindness

A service man is classified as blinded or industrially blinded when central vision in the better eye is reduced to 20/200 and is not correctable, or when peripheral vision is reduced to 20 degrees or less

even though central vision is better than 20/200.

Low vision. An individual classified as blinded is referred to as having low vision when, in the better eye, vision ranges between moving objects and 2/200. Those having light perception only are, for practicable purposes, classified with the totally blinded.

Useful vision. An individual classified as blinded is referred to as having useful vision when, in the better eye, vision ranges from 3/200 to 20/200, whether it be central, peripheral, or both. In general, it is considered that individuals falling in this group can engage in various types of occupations in a manner approaching the sighted, and travel about the country without an escort. Their efficiency in this respect naturally increases in proportion as vision nears 20/200.

Places where blindness was incurred

In so far as this report is concerned the European Theater of Operations includes England, Iceland, Greenland, France, Germany, Holland, and Belgium. The Mediterranean Theater includes North Africa, Italy, and the Middle East. The Pacific Theater includes all areas in which the Japanese were engaged in action, and the Zone of the Interior refers to the continental limits of the United States.

Blinded, residual of enemy action. Of the 367 blinded considered in this report the following percentages occurred as the result of enemy action:

European Theater	162 (44.14%)
Mediterranean Theater	46 (12.53%)
Pacific Theater	26 (7.08%)
Total	234 (63.76%)

Enemy agents through which blindness was incurred were as follows:

Booby-trap explosion	9
Bullet, machine gun, and rifle	32
Bazooka-shell explosion	5
Concussion, exploding shells, no external injuries	2
Flack and gun fire from enemy plane	5
Hand- and rifle-grenade explosion	13
Land mine explosion	41
Mortar-shell explosion	26
Shrapnel	24
Shell fragments, type of shells unknown	74
V-2-bomb fragments	1
Total	234

Blinded, residual of accident. Of the cases of accidental blindness, 37 can be justly classified as incidental to training. Accidental blindness was incurred in the various theaters as follows:

European Theater	14 (3.81%)
Mediterranean Theater	7 (1.91%)
Pacific Theater	11 (2.99%)
Zone of the Interior	36 (9.80%)
Total	68 (18.51%)

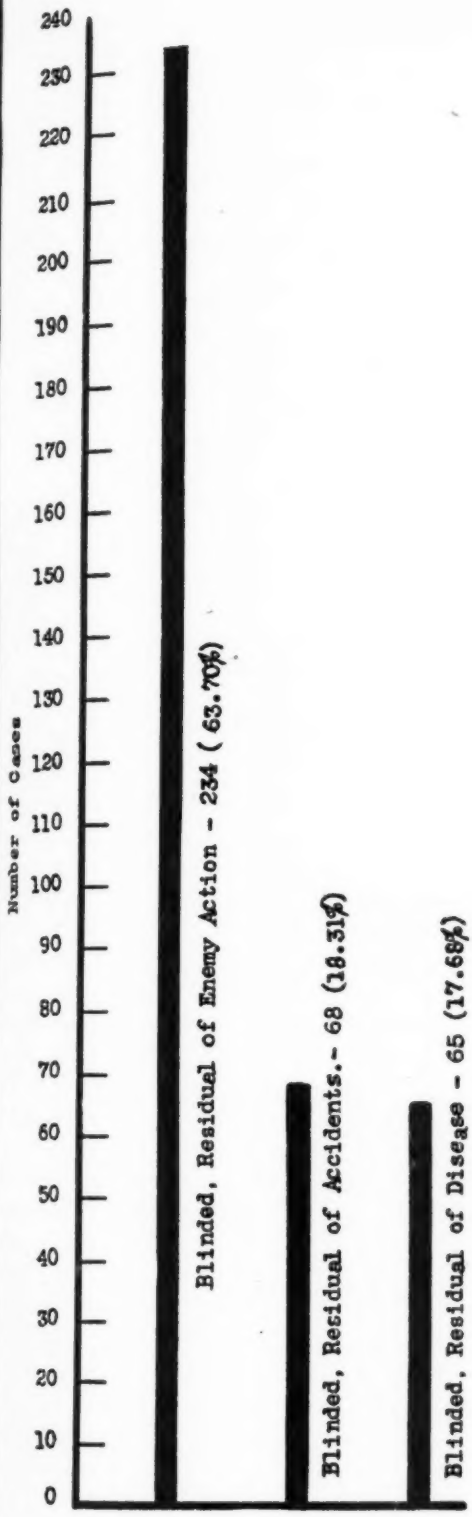
The following types of accidents resulted in blindness:

Airplane crash	1
Ammunition explosion (shells, cartridges)	8
Booby-trap explosion	4
Blasting-cap explosion	3
Dynamite explosion (catching fish for mess)	4
Dynamite explosion	4
Detonator-cap explosion	2
Gasoline fumes (high-octane gas, containing lead)	2
Gun shot	6
Grenade explosion	3
Knife wound, opening can	1
Kicked in face by mule	1
Land-mine explosion	3
Motor-vehicle accident	3
Methyl alcohol, ingestion of	14
Retinitis, solar	1
Struck in face with stick	1
Struck in eye with wrench	1
Struck in eye with garden hose	1
Struck in face with bottle	1
Struck by lightning	1
TNT explosion	3
Total	68

Blinded, residual of disease. Blindness as a result of disease occurred in:

European Theater	10 (2.72%)
Mediterranean Theater	4 (1.09%)

Number of Cases



Pacific Theater	7 (1.91%)
Zone of the Interior	44 (11.98%)
Total	65 (17.70%)

Diseases through which blindness was incurred were as follows:

Atrophy of the optic nerve, cause obscure	14
Atrophy of the optic nerve, following trypanosamide therapy	1
Atrophy of the optic nerve, residual of brain tumor	1
Atrophy of the optic nerve, residual of encephalomyelitis following vaccinia	1
Atrophy of the optic nerve, residual of retrobulbar neuritis following spinal anesthesia	1
Atrophy of the optic nerve, residual of epidemic cerebro-spinal meningitis	2
Atrophy of the optic nerve, residual of beriberi contracted in Japanese prison camp	4
Choroido-retinitis, syphilitic	1
Choroido-retinitis, cause obscure	6
Degeneration, macular	9
Gun-shot wound, self-inflicted	1
Keratitis, interstitial	1
Neuritis, retrobulbar, cause obscure	7
Retinitis, hemorrhagic	2
Retinitis, hemorrhagic (Eales's disease)	2
Retinitis proliferans	1
Retinitis pigmentosa	6
Sclerosis, multiple	2
Thrombosis, cilioretinal artery	1
Uveitis	1
Total	65

Eleven cases of blindness as the result of enemy action were due to occipital-lobe injuries without complicating injuries to the optic nerves or globes.

In the case of blindness due to injury incident to opening a can with a knife, the patient had, at the time of injury, a macular degeneration of the other eye with vision reduced to counting fingers at 12 inches. The injured eye was enucleated.

In one case of blindness due to gunshot wound of the eye, the patient had undergone an enucleation of the other eye prior to the accident.

Chart 1 (Thorne). Showing whether blindness was due to enemy action, accident, or disease.

The patient who had been blinded by a blow in the eye with stick had an amblyopia ex anopsia of the other, with vision reduced to 2/200.

The patient who was blinded by a blow in the eye with a garden hose had an amblyopia ex anopsia of the other, with vision reduced to 20/200.

The patient blinded by being kicked in the eye by a mule had an amblyopia ex anopsia of the other, with vision reduced to 4/200.

In the case of blindness caused by thrombosis of the cilioretinal artery, the patient had undergone, prior to onset, an enucleation of the other eye.

Two cases of blindness caused by concussion induced by exploding shells pre-

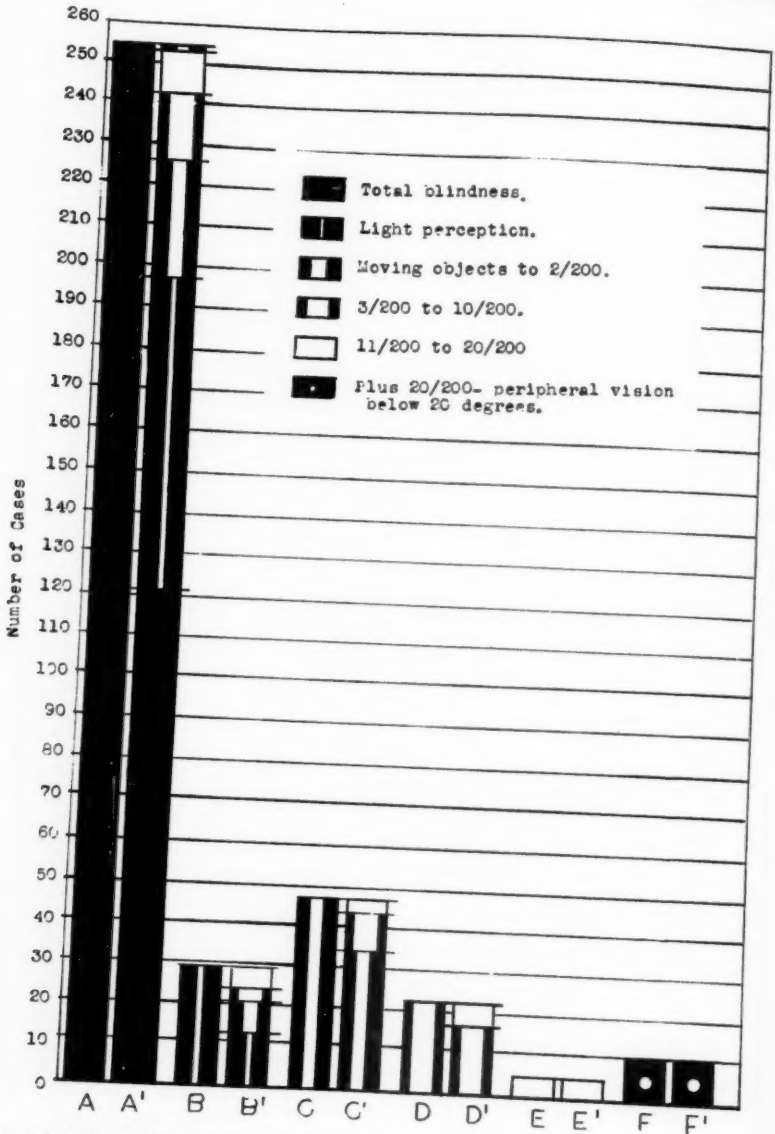


Chart 2 (Thorne). Degree of blindness encountered in the 367 cases considered.

sented bilateral macular degeneration with normal peripheral vision as to extent.

The patient who was blinded by being struck by lightning presented bilateral optic-nerve atrophy as a residual.

In the case of blindness due to a blow in the eyes with a bottle, one eye had to be enucleated and a massive detachment of the retina occurred in the other; vision was reduced to light perception.

The patient whose blindness was due to a blow in the eye with a wrench had a high myopia of the other eye with vision reduced to 4/200.

One case of blindness which occurred in the Pacific Theater was due to a self-inflicted gun-shot wound of the orbits during a period of acute mental depression.

Of the 367 patients considered, 47 (12.80 percent) had both eyes enucleated, one had both eyes eviscerated, and 147 or 40.05 percent had one eye enucleated. Binocular phthisis bulbi was found in 18 (or 4.90 percent), and monocular phthisis in 66 (or 17.98 percent).

A more detailed explanation of chart 2 follows:

Columns A and A′ give data on 254 blinded or industrially blinded service men, A representing one eye and A′ the other of the same individuals. A indicates that the 254 (69.20 percent) were totally blinded in one eye, while A′ indicates that 121 (32.97 percent) were totally blinded in the other eye as well. Of the remaining 133 in the A′ column, 76 (20.79 percent) retained light perception; 29 (7.71 percent) retained vision ranging from moving objects to 2/200; 16 (4.35 percent) retained vision ranging from 3/200 to 10/200; 11 (2.99 percent) retained vision ranging from 11/200 to 20/200, while 1 (.27 percent) retained vision better than 20/200 but with peripheral vision reduced to 20 degrees or less.

Columns B and B′ give data on 29 industrially blinded service men, B representing one eye and B′ the other of the same individuals. B indicates that 29 (7.90 percent) represented retained light perception in one eye while B′ indicates that 13 (3.81 percent) of these retained only light perception in the other eye as well. Of the remaining 16 in column B′, 8 (2.17 percent) retained vision ranging from moving objects to 2/200; 3 (.81 percent) retained vision ranging from 3/200 to 10/200; while 5 (1.36 percent) retained vision ranging from 11/200 to 20/200.

Columns C and C′ give data on 47 industrially blinded service men, C representing one eye and C′ the other of the same individuals. C indicates that the 47 (12.80 percent) retained vision ranging from moving objects to 2/200 in one eye, while C′ indicates that 34 (9.26 percent) retained the same range of vision in the other eye as well. Of the remaining 13 in column C′, 9 (2.45 percent) retained vision ranging from 3/200 to 10/200, and 4 (1.09 percent) retained vision ranging from 11/200 to 20/200.

Columns D and D′ represent 22 industrially blinded service men, D representing one eye and D′ the other of the same individuals. D indicates that the 22 (5.99 percent) represented retained vision ranging from 3/200 to 10/200 in one eye, while D′ indicates that 17 (4.63 percent) of these retained the same range of vision in the other eye as well.

Of the remaining 5 (1.36 percent) in the D′ column, all retained vision ranging from 11/200 to 20/200.

Columns E and E′ represent five industrially blinded service men, E representing one eye and E′ the other of the same individuals. E and E′ indicate that the 5 (1.36 percent) represented retained vision in both eyes ranging from 11/200 to 20/200.

Columns F and F′ represent 10 industrially blinded service men, F representing one eye and F′ the other of the same individuals. F and F′ indicate that the 10 (2.72 percent) represented retained central vision better than 20/200 in both eyes, but with peripheral vision reduced to 20 degrees or less.

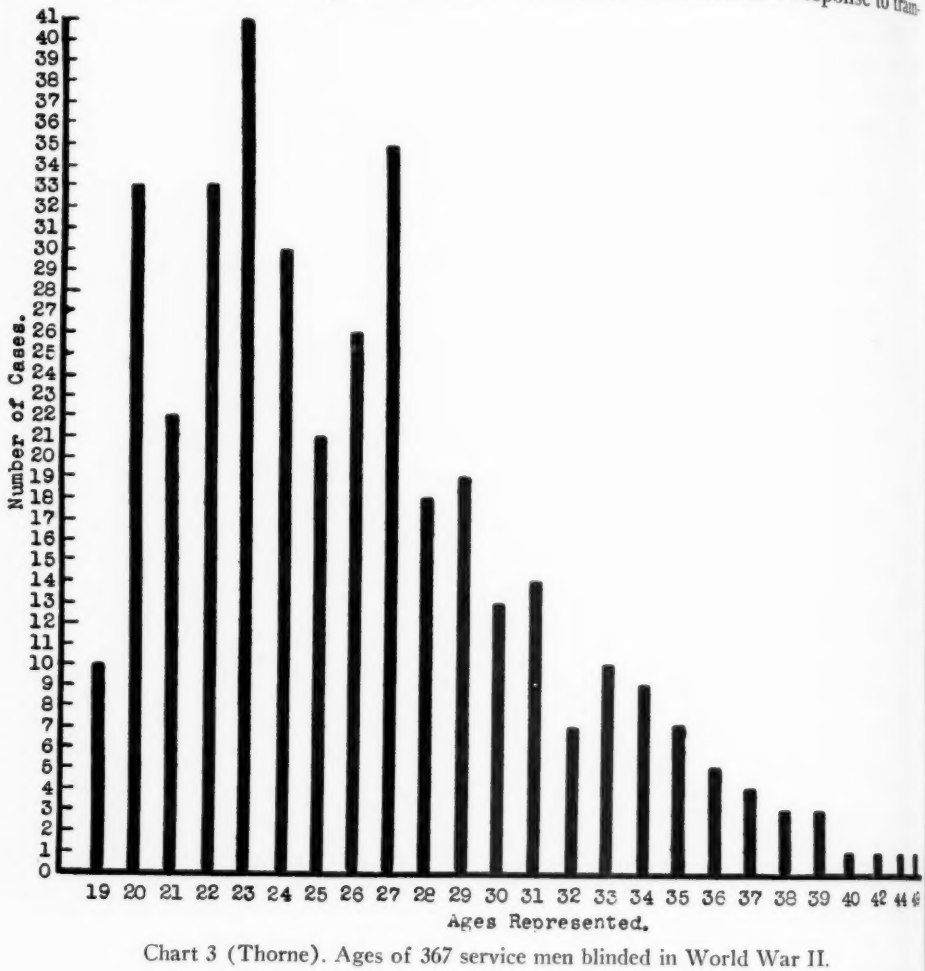


Chart 3 (Thorne). Ages of 367 service men blinded in World War II.

In chart 3, it will be noted that of the 367 service men who were blinded 288 (78.47 percent) were below 30 years of age.

Response to training

This portion of the report, which is concerned with training, considers only 202 consecutive admissions, this being the number of men who had completed training and were separated from the service at the time this report was prepared.

The following standards were used to evaluate an individual's response to training: (1) Ability to orient well. (2) Determination to accept a minimum of assistance. (3) Eagerness for activity, both social and vocational. (4) Control of unwholesome antisocial habits. (5) Genuine self-confidence in capabilities and self-assurance in ability to hold a job. (6) Insight into limitations and potentialities. (7) Ability to get along with others in the community.

In rating individuals according to these standards, a seven-point score was used: Superior, excellent, very satisfactory, satisfactory, unsatisfactory, unadjustable, and incorrigible.

It will be noted in chart 4 that of the 202 blinded men whose training was completed, 160 (79.37 percent) were given a rating of satisfactory or better in respect to the results of training for rehabilitation.

A rating of unsatisfactory was given when it was felt that the blinded man did not quite measure up to the standard established and could not be considered as adjusted to his blindness. However, it was considered possible, and in some cases quite likely, that a satisfactory adjustment would eventually be made.

Of those given the grade of unsatisfactory, defects such as the following were frequently found by the psychologist: "Confused and fearful, poor home environment, poor background, irresponsible, immature, and chronic alcoholism." The average score attained by this group in the Army General Classification Test was 86.4, the highest score attained being 124 and the lowest 54. Two trainees in this group attained the score of 124. One of these had sustained a severe brain injury and was disturbed, fearful, and anxious. The other was immature, confused, and unrealistic. The trainee who attained the score of 54 was unstable, irresponsible, and had a poor home background. The average score attained in the Wechsler-Bellevue Test was 102, the highest score being 124 and the lowest 73.

The rating of unadjustable was given when the blinded man was considered to be not adjusted, and further, not adjustable nor trainable. Mental defectives and those severely disturbed emotionally were placed in this category.

Of those given the grade of unadjustable, defects such as the following were frequently found by the psychologist: "Rejects blindness, mental defective, severe brain injury, and psychoneurotic." The average score attained by this group in the Army General Classification Test was 65.7, the highest score being 95 and the lowest 39. The trainee whose score was 95 was a hypochondriac, was fearful

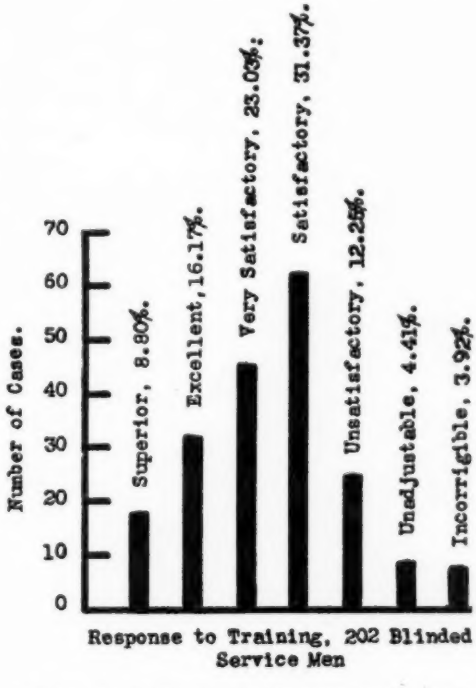


Chart 4 (Thorne). Ratings of 202 blinded service men with respect to training for rehabilitation.

and dependent; and the trainee who attained the score of 39 was mentally defective and a psychoneurotic. The average score attained by this group in the Wechsler-Bellevue Test was 84.2, the highest score being 104 and the lowest 62.

The rating of incorrigible was given when the blinded man displayed antisocial behavior patterns or serious alcoholism.

Of those given the rating of incorrigible, defects such as the following were commonly found by the psychologist:

"Psychopathic, psychoneurotic, emotionally disturbed, alcoholism, and delinquent." The average score attained by this group in the Army General Classification Test was 86.5, the highest score being 98 and the lowest 72. The trainee who attained the score of 98 was a delinquent, was psychopathic, and a chronic alcoholic; and the trainee who attained the score of 72 was a chronic alcoholic. The average score attained by this group in the Wechsler-Bellevue Test was 102.1, the highest score being 120 and the lowest 95.

Summary

Number of blinded upon which report is based	367	
Blinded, result of enemy action	234	(63.76%)
Blinded, causes other than enemy action (accident and disease)	133	(36.21%)
Totally blinded and retaining light perception only	210	(57.22%)
Low vision retained (vision of little or no value)	71	(19.34%)
Useful vision	86	(23.42%)
Both eyes enucleated or eviscerated	47	(12.80%)
One eye enucleated	147	(40.05%)
Phthisis bulbi, both eyes	18	(4.90%)
Phthisis bulbi, one eye	66	(17.98%)
Number of blinded below 30 years of age	288	(78.47%)
Percentage of blinded who made a satisfactory or better adjustment	79.37%	
Percentage of blinded who made an unsatisfactory adjustment	12.25%	
Percentage of blinded considered as unadjustable	4.41%	
Percentage of blinded considered as incorrigible	3.92%	

950 Grayson Street (8).

NOTES, CASES, INSTRUMENTS

OPERATIVE PROCEDURE FOR SUBLUXATED LENS

WILLIAM M. COCKRUM, M.D., AND HOWARD C. SLAUGHTER, M.D.
Evansville, Indiana

The subluxated lens, or tremulous lens, according to Duke-Elder,[1] occurs when the suspensory apparatus is weakened so that the lens becomes tremulous, or subluxated, but remains within the pupillary aperture. This is to say that some of the suspensory ligament does not remain intact. The usual surgical procedure for the removal of such lenses is by spoon or loop extraction or, if the patient is younger, by discission. Dutt[2] discussed the nonviolent delivery of the subluxated lens by the lever-action intracapsular route. By this method, the lens is removed from the anterior chamber after iridectomy by rotating it through the corneal wound, using the attached zonule as the fulcrum and providing pressure on the globe below. Knapp's[3] paper on the operative treatment of congenital subluxated lens reviews the types of operations from which to choose. The first was an iridectomy to give a clear zone in the aphakic area through which to see. The second is discission, which is very difficult because the lens eludes the end of the knife; there is no tension on the capsule; and the opening is small. Moreover, the incision does not remain open, and several operative procedures are usually necessary. Knapp states that needling should be done in adolescence only. The third choice is removal of the lens by spoon or loop extraction. The indications for operation are cyclitis, glaucoma, or poor vision.

The procedure under discussion consists of the usual keratome incision with McLean suture. The incision is enlarged with the scissors. Iridectomy is then performed at the 12-o'clock position with the use of a blunt iris hook to engage the iridic margin. The iris is drawn up into the incision and the iridectomy performed. During the entire operative procedure, it is necessary that the assistant hold the lids away from the globe. After the iridectomy is performed, an Arruga forceps is used to enter the anterior chamber; the upper margin of the subluxated lens is grasped, and the lens withdrawn from the anterior chamber by the intracapsular route.

The causes for subluxation of the lens can be congenital, traumatic, and consecutive or spontaneous. The findings are a deep anterior chamber, iridodonesis. The convex edge of the lens can usually be seen in some part of the pupillary aperture. Monocular diplopia may be present.

REPORT OF CASE

A white man, single, aged 37 years, was first seen in the office on December 30, 1944. He said that he had had poor vision in his left eye for a number of years and, about four weeks previous to this date, the visual acuity in his right eye suddenly diminished. The eye had been moderately red since that date. The patient did not report loss of vision in his left eye. He did not have monocular diplopia. He had not suffered trauma but had been doing heavy labor, part of which consisted of carrying 100-lb. sacks on his shoulders. This, we think, could traumatize a congenitally weak suspensory apparatus sufficiently to allow the lens to subluxate.

On examination, it was found that this man had a bilateral dislocation of both lenses. The anterior chamber was deep and iridodonesis was present. The superior margin of the lens could be seen in

each eye, covering about two thirds of the pupillary aperture. The pupil of the right eye was widely dilated and fixed to light, but the left eye was normal in size and reacted to light. There was a mild ciliary congestion of the right eye. The tension in the right eye was 15 mm. Hg (Schiøtz); in the left eye 13 mm. The fundus, viewed through the aphakic portion, appeared normal in both eyes.

The patient was not wearing glasses. His vision, with squinting, was 20/300 in the right eye; 20/200, in the left. Atropine, to be used twice a day in the right eye, was prescribed, and the patient was advised to use hot packs and return on January 2d for the surgical removal of the dislocated lenses.

Family history revealed that this man's maternal grandmother had undergone an operation for dislocated lenses 50 years ago. His mother and two of his uncles had dislocated lenses. The mother had an operation on both eyes, one of them successful, about 40 years ago. One of the uncles had also been operated upon successfully about 40 years ago. The second uncle was under regular observation by a physician. The patient had six brothers and one sister. Two of the brothers had dislocated lenses but refused operative procedures, for they were comfortable and had good vision with glasses. A family characteristic was height of about 6 ft.

Physical examination revealed a tall, thin man, weight 145 lbs. (65.9 kg.), height 73 in. (185 cm.), with a long, thin trunk and arms of greater than normal length. This patient fits the description of Marfan's syndrome.

On January 2d, the lens of the left eye was extracted under local anesthesia. During the operative procedure, the lens tilted into the anterior chamber and was very easily grasped with the Arruga forceps and removed. It was not necessary to assist the removal of the lens in any other way. The position of the lens was viewed through the cornea, not by direct vision. A bead of vitreous showed in the wound at the conclusion of the operation. However, it was not cut off, and the eye was bandaged with a dry dressing. The dressing was changed on the second postoperative day. The prolapse of vitreous was not marked, but had increased somewhat and, on the third postoperative day, the protruding vitreous was touched with a heated muscle hook.

The patient was very anxious to have the lens removed from his right eye. On January 8th, a similar operation was performed on the right eye without prolapse of vitreous. A McLean suture sealed the wound satisfactorily. The postoperative course was uneventful, and the patient was discharged from the hospital on January 13th, with some gaping of the wound of the left eye at the point of the prolapse of the vitreous. He was not seen again until January 22d, when vision was: R.E. with a +13.00D. sph., 20/50; L.E., with a +13.75D. sph. ⌒ −2.75D. cyl. ax. 60°, 20/40. He still had some irritation of the right eye. He was given atropine; and also typhoid antigen H (20 million organisms) intravenously.

He was then seen at weekly intervals, and the right eye gradually cleared. He wore temporary lenses in the form of spheres until April 13th, when permanent lenses were prescribed. Vision was: R.E., with a +14.25D. sph. ⌒ −1.25D. cyl. ax. 110°, 20/40; L.E., with a +14.75D. sph. ⌒ −1.25D. cyl. ax. 45°, 20/30. An addition of +2.75 D. sph. was given for close work. Binocular vision, was 20/25–2. The patient stated that he saw better than he ever had in his life.

908-9 Hulman Building (18)

References

[1] Duke-Elder, W. S. Text book of ophthalmology. St. Louis, C. V. Mosby Co., 1941, v. 3, p. 3238.
[2] Dutt, K. C. Extraction of subluxated lens made non-violent by lever action intracapsular operation. Arch. of Ophth., 1939, v. 22, Nov., pp. 844-848.
[3] Knapp, Arnold. Operative treatment of congenital subluxation of lens. Arch. of Ophth. 1942, v. 27, Jan., pp. 158-160.

UNUSUAL COMPLICATION OF SPHENOPALATINE BLOCK

VICTOR GOODSIDE, CAPT. (MC), A.U.S., AND SAMSON WEINGEIST, CAPT. (MC), A.U.S.

Fort Bragg, North Carolina

The present report is concerned with a complication of sphenopalatine, or maxillary-nerve block, evidently not of frequent occurrence. In performing this procedure, it has been customary in our experience to enter the needle into the palatine foramen in an upward direction, passing it through the pterygopalatine canal into the pterygopalatine fossa to a depth of about 3 cm. From 2 to 2½ c.c. of a 1-percent solution of novocaine is usually injected. The anesthesia produced is useful in dental surgery; in nasal surgery, both alone and as an adjunct to topical application of cocaine; in the treatment of sphenopalatine neuralgia; and, finally, in the treatment of ocular pain. It is possible for the needle, if carried too far, to pass through the pterygopalatine fossa into the inferior orbital fissure. The effects obtained when this occurs will depend on the precise site of deposition of the anesthetic agent. Two cases are here presented in which temporary paralysis of the external rectus muscle was produced by the injection described.

Case 1. Novocaine (2½ c.c. of a 1-percent solution) was injected on the left side in the manner described as preliminary to dental surgery. Five minutes later, the patient complained of double vision. On examination, 15 minutes later, he was found to have complete paralysis of the external rectus muscle on the side injected. There was complete corneal anesthesia. The pupil was slightly irregular, somewhat larger than that of the fellow eye, and slightly sluggish in response to light and accommodation. Ocular examination was otherwise completely negative. Two hours later, the diplopia was no longer in evidence; ocular movements were normal in all directions of gaze; corneal sensitivity had returned; and the pupils were equal and regular and responded actively to light and accommodation.

Case 2. A patient received an injection of 1 c.c. of a 1-percent solution of novocaine and of 1 c.c. absolute alcohol into the pterygopalatine fossa in treatment for sphenopalatine neuralgia. Almost immediately, the patient complained of double vision. Examination revealed complete paralysis of the external rectus muscle. Pupils were equal and regular and reacted to light and accommodation. Corneal reflexes were retained. The paralysis of the external rectus receded gradually over a period of two days. The patient was returned to duty nine days later without complaint.

Regional Station Hospital.

RECURRENT DETACHMENT OF THE CHOROID FOLLOWING TREPHINING OPERATION*

JAMES W. SMITH, M.D.
New York

In 1868, Herman Knapp diagnosed sarcoma of the choroid in an eye following cataract extraction which, on section, proved to be a choroidal detachment. Similar reports by competent ophthalmologists have appeared as recently as 1934. Operations or injuries that induce marked reduction in intraocular pressure have long been recognized as occasionally giving rise to choroidal separation. This separation was looked upon as a transient phenomenon that disappeared in several days following wound closure and the establishment of normal intraocular pressure.

When Elliot's trephining operation for chronic noninflammatory glaucoma gained acceptance, observers reported that choroidal separation not only occurred frequently, but that the detachments often were of longer duration. Prior to the use of corneoscleral sutures, few observers had the courage to examine fundi earlier than one week after cataract extraction, whereas ophthalmoscopy sooner after trephination was entirely safe. O'Brien[1] found transient separation of the choroid in 93 percent of his cataract-extraction series. Although Elliot admitted reluctantly that the complication occurred in about 3.5 percent of trephining operations, the reports of Bothman and Blaess,[2] Rycroft,[3] and Rubert[4] showed an incidence varying from 14 to 50 percent.

According to Fuchs, a rent in the perichoroidal space followed by transudation of fluid from the choroidal vessels produces the detachment which disappears when the leaking surgical section heals firmly. Spaeth and DeLong[5] believe that choroidal detachment "may be due to massive edema, a disturbance of the perichoroid or hemorrhagic choroiditis or a combination of the three conditions." They suggest "massive perichoroidal edema" as a more correct designation for postoperative and posttraumatic conditions not essentially hemorrhagic.

It is generally accepted that most postoperative detachments of the choroid disappear completely within three to seven days. However, many cases are reported of anterior chambers that remained open for six weeks or even six months with persistence of the choroidal separation. Stress has not been laid upon the danger of such a prolonged complication. Failure of the anterior chamber to re-form creates an abnormal situation giving rise to low-grade uveitis, synechia in the anterior angle, and lens-capsule and cortex opacities. Persistent detachment of the choroid is delineated by pigment granules and streaks seen ophthalmoscopically, and later by actual degenerative changes in the choroid and retina. Secondary hemorrhage and absolute glaucoma may develop, causing blindness and necessitating enucleation.

In view of these possibilities, concern must be expressed at the therapeutic suggestions appearing in ophthalmic textbooks. For treatment of choroidal separation Berens advises "keeping the patient in bed;" Elliot recommends "getting the patient out of bed;" and Parsons dismisses the subject by stating that "most patients get well without treatment." Verhoeff and others recommend scleral puncture to effect reposition by withdrawing serous fluid in the perichoroidal space. The procedures having the soundest surgical basis are cauterization of the tre-

* From the Department of Ophthalmology, New York Post Graduate Medical School and Hospital, Columbia University.

Read in part before the New York Society for Clinical Ophthalmology, February 5, 1945.

phined bleb or covering it with a flap of conjunctiva or a strip of superior-rectus tendon. Disagreement exists regarding the safe period before effecting closure of a fistulizing wound. Rycroft believes that a trephine leak should be sealed off after seven days, whereas Duke-Elder suggests repair if the choroidal detachment has persisted for three months!

A warning should be sounded against these extreme views. The danger of prolonged bed rest, particularly in aged patients, cannot be overemphasized. In addition, the upright position, by gravity, decreases the amount of fluid lost through the open wound. Intervention seven days postoperatively is unwarranted. I know of one case wherein premature and excessive cauterization precipitated a fresh attack of glaucoma. Excessive delay for three months can lead only to the complications mentioned above. Choroidal separation and failure of the anterior chamber to re-form two weeks after trephination must be regarded seriously. Mild cauterization of the conjunctival wound edges is indicated and may be repeated every third day if necessary. When this treatment is not effective within two weeks, the trephine bleb should be covered with a flap of conjunctiva or superior-rectus tendon.

Case report

A 1½-mm. trephination of the right eye (May 4, 1943) was effective in reducing intraocular pressure for six weeks and, despite daily use of miotics, the pressure was controlled for only one year. On June 9, 1944, a 2-mm. trephining operation was performed 4 mm. temporal to the former site. The globe was too soft for accurate ophthalmoscopy until the sixth day, when detachment of the choroid was observed in the inferior portion rising almost to the inferior edge of the optic nerve. Two days later the anterior chamber re-formed, the choroid appeared to be replaced, the patient left the hospital, and vision improved from perception of fingers to 20/100. After six days, detachment again occurred which lasted 48 hours. On July 4th, excessive tearing was present, followed by visual veiling and distortion which persisted for 12 hours.

The fourth detachment on July 21st cleared in two days, with recovery of vision to 20/50+2. Two transient spells of tearing, veiling, and distortion were observed by the patient in August. The fifth and last detachment was seen on September 11th, three months after the operation.

Vision in the left eye with glaucomatous optic-nerve atrophy was 3/200 in a 15-degree temporal sector only. Some apprehension was felt regarding the ultimate outcome in the patient's only useful eye. Procedures considered were cauterization of the bleb and Magitot's[6] operation for covering trephine opening with a strip of superior-rectus tendon. The possibility of wound closure with return of glaucoma suggested that conservatism would be the wiser choice. Treatment, therefore, was limited to continual *ad maximum* dilatation of the pupil of the right eye, using 1-percent atropine followed by paredrine three times daily. The outstanding clinical finding observed since the operation was the appearance of a fixed arc of pigment granules corresponding to the summit of the choroidal detachment. The nasal half of this pigment line disappeared after two months, and at present only several fine pigment dots are noted in the choroid 2½ disc diameters inferior to the optic nerve, with evidence of thinning of the choroid due to atrophy. Hypotony was present for four months, when a small bleb appeared over the site of trephination and the tension rose to 20 mm. Hg

(Schiøtz), which has been maintained to date. The field of vision is fuller at present than it was preoperatively, and there is a 15-degree contracture superonasally and one 20 degrees superotemporally. Three diopters of myopia[7] have developed since operation, and with full correction the vision is 20/50— due to the sclerosis of the lens nucleus, which was noted before operation. At first dressing an interesting clinical finding was the almost complete loss of the normal upper-lid convexity. This defect has persisted to a lesser degree and is probably associated with a loss of scleral curvature about the zone of operation.

1016 Fifth Avenue (28).

References

[1] O'Brien, C. S. Further observations on detachment of the choroid after cataract extraction. Arch. of Ophth., 1936, v. 16, p. 655.
[2] Bothman, L., and Blaess, M. J. Results of the surgery of glaucoma. Amer. Jour. Ophth., 1936, v. 19, p. 1073.
[3] Rycroft, B. W. Choroidal detachment. Brit. Jour. Ophth., 1943, v. 27, p. 283.
[4] Rubert. quoted by Rycroft.
[5] Spaeth, E. B., and DeLong, P. Detachment of the choroid. Arch. of Ophth., 1944, v. 32, p. 237.
[6] Bothman, L. Repair of choroidal detachment. Arch. of Ophth., 1937, v. 18, p. 65.
[7] Smith, J. W. Progressive refraction changes following trephine operation. Arch. of Ophth., 1933, v. 9, p. 259.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

October 18, 1945

DR. WARREN S. REESE, *chairman*

NEUROFIBROMATOSIS IN THREE CONSECUTIVE GENERATIONS

DR. EDITH HARVEY (by invitation) presented the case of a girl, 5 years of age, who entered the clinic, with a history of gradual protrusion and deviation downward of her left eyeball. She was an intelligent, healthy child, having had none of the usual childhood diseases except occasional colds. A tonsillectomy had been performed the previous year.

On examination, there was an exophthalmos of the left eye measuring 3 mm., with the visual axis directed downward 30° and temporally 5°, while the visual axis of the normal eye was directed straight forward. Ocular rotations were fairly good in all fields except that of the superior rectus, in which there was definite limitation. Visual acuity was 20/30 in the normal eye and 1/200 in the exophthalmic eye. There was a definite unilateral papilledema in the left eye. She had café-au-lait pigment spots on her chest and abdomen, but no subcutaneous neurofibromata.

Blood count and urinalysis were normal, as were the serum, calcium, and phosphorus determinations.

Roentgenographic studies of the orbit showed no bone involvement, except some slight enlargement of the optic foramen on the involved side. The sphenoidal ridges were normal, and the bones of the skull showed no abnormalities. There was no evidence of calcification. Roentgenographic studies of the sinuses were normal.

The patient was operated upon by Dr. E. B. Spaeth. A neurofibroma was found encircling the entire intraorbital portion of the optic nerve from its exit from the eyeball to the optic foramen. The eyeball and optic nerve up to the foramen were removed. The tumor mass, which was about 9 mm. in diameter along the entire length of the nerve, seemed to be constricted to the normal size of the nerve at the optic foramen, and it is to be hoped that it did not involve the intracranial portion of the nerve.

No other tumor masses were palpable in the orbit.

Microscopic sections of the enucleated eyeball and optic nerve showed an intact, undamaged optic nerve with a pure fibroma, containing no nerve fibers, surrounding it. There was, in addition, edematus infiltration of the nerve heads. The slides of these sections were discussed later in detail by Dr. DeLong, under whose direction they were made and carefully studied.

The mother of the child had multiple, cutaneous neurofibromata, most numerous over her back, but scattered also on her abdomen, neck, and extremities. Many had been present since birth; others appeared at puberty. She had a few café-au-lait spots on her abdomen. One of the tumor masses on her arm was removed, and the microscopic diagnosis was neurofibroma. When a similar tumor had been removed some years previously, the same microscopic report had been given.

The child's grandfather, on the maternal side, had died at the Presbyterian

Hospital. He had had a suboccipital craniotomy for neurofibromatosis of the middle and posterior fossae. Necropsy findings included: generalized neurofibromatosis, gastric subserous neurofibroma, and a cervical perineural fibrosarcoma.

The antecedent relatives lived in Norway, and the only history obtainable was the recollection of the child's mother that she had heard that her own grandmother, on the paternal side, had had several nodular masses on her face. Whether these were neurofibromata is, of course, impossible to determine.

The brother of the child, and the sisters and brothers of the mother, have no known abnormalities suggestive of neurofibromatosis.

Dr. Harvey pointed out that neurofibromatosis is an hereditary and sometimes familial condition characterized by skin lesions and tumors on nerves. These lesions she discussed in detail, and presented a brief résumé of the general symptoms.

She also stated that this disease is congenital, showing Mendelian dominance in successive generations, although occasionally one is skipped. There is no sign of sex-linked inheritance.

There seems to be a congenital defect which exists in the nerve-sheath tissue, resulting in a hyperplasia of the nerve-sheath connective tissue, the cells being adult in type and not embryonic. The stimulus for hyperplasia is present from birth. New tumor masses may appear at puberty, pregnancy, or with intercurrent infections. They are not stimulated by local trauma.

The origin of these tumors has been a matter of controversy which is still not settled. Von Recklinghausen believed that the tumors were mesoblastic in origin, arising from the endoneurium. Verocay considered them as ectodermal derived from the cells of the sheath of Schwann. According to Penfield and Young they are the result of a connective-tissue reaction about the fibers of the nerves, and show both nerve fibers and connective-tissue elements, although the differentiated fibroblast, and not glial cell, is the typical cell. Whether cells of the sheath of Schwann are specialized glial cells or not is still a disputed question.

Sarcomatous changes have frequently occurred in neurofibromatosis. Operative removal of a neurofibroma may be followed by the recurrence of a benign neurofibroma. On the other hand, sarcomatous transformation may occur at the site of removal or in a distant preëxisting fibromatosis nodule. Metastasis is relatively infrequent, when a benign neurofibroma becomes sarcomatous; instead it is followed by transformation into sarcoma of a neurofibroma in another part of the body.

Discussion. Dr. Perce Delong said that this multiple tumorous syndrome is a disease of congenital origin characterized by cutaneous pigmentation and multiple tumors of cranial and peripheral nerves. The growths in Von Recklinghausen's disease are not true neuromas, which must consist of both nerve tissues and nerve cells, hence the term neurofibromatosis.

Penfield and Young, in describing the involvement of the nerve trunks, meninges, and central nervous system, state that there is found a definite hyperplastic reaction of the cells peculiar to these tissues, indicating that there must have been an irritant or stimulating influence exerted on these tissues, causing hyperplasia, which is followed by true neoplastic growth of these cells.

This specimen does not differ from those reported. The clinical, ocular signs are secondary. These are: exophthalmos, due to pressure from behind; choked disc, due to pressure; degeneration; and optic atrophy. Van der Hoeve is the only one

who reported an ocular manifestation involving the retina.

Pathologic change in this case showed the tunics of the globe to be normal with the exception of one ciliary nerve which presented some edema of the nerve with a thickening of its sheaths. There was also an early papilledema of the nerve head.

The optic nerve presents marked edema of the nerve and definite fibrosis of the sheaths. The hyperplasia is most marked in the region of the arachnoid, giving the nerve the appearance of being about twice its size. Microscopically, no cellular elements are present, but marked hyperplasia and fibrosis of the nerve sheaths.

Dr. E. B. Spaeth said that he again wished to call special attention to the matter of development of sarcoma in neurofibromatosis. He had recently seen two additional cases. The first patient presented before this group about two years ago with neurofibromatosis in the upper division of the 5th nerve, now had developed sarcomatous changes accompanied by severe hemorrhages.

The second patient had a neurogenic sarcoma which seemed to arise in an otherwise benign neurofibroma of the orbit.

The astonishing feature in the cases presented by Dr. Harvey was that one will probably never see three more dissimilar instances of a common hereditary process. In the first case, that of the grandfather, there was a neurogenic sarcoma (sarcomatous changes from neurofibromatosis). In the second case, that of the mother, the lesions were confined purely to the skin. In the third case, the child's, there was a neurofibroma of the optic nerve, itself.

Dr. Francis H. Adler asked Dr. Harvey whether this tumor did not originate in the sheath of the nerve, not the nerve fibers. He added that he would like to point out that the theory that these tumors start in the neurilemmal sheath must be wrong, at least in the case of the optic nerve, because the optic nerve fibers, like the fiber tracts of the brain, have no neurilemmal sheath. It is not a true sensory nerve.

Dr. Edith Harvey replied that it is now generally believed that neurofibromats arise from the connective-tissue sheaths of the nerves, and not from the neurillemma; that is, they are mesodermal in origin.

A possible early case of ocular pemphigus

Dr. Joseph V. Klauder (by invitation) and Dr. Alfred Cowan presented the case of a white woman, aged 29 years, who, since February, 1944, had had recurring erosive areas on the buccal mucosa, the lips, under the tongue, and on the floor of the mouth. These areas disappeared and reappeared at intervals of a few weeks to a few months. When lesions appeared on the lips, she observed that the initial manifestation was a blister which soon ruptured, leaving a crusted surface.

In July, 1945, when first seen, she had a cutaneous outbreak. This was the first time such lesions appeared. On each elbow there was a bleb which was partially collapsed. The skin around the bleb was normal. There was a similar lesion near the external canthus of the right eye. The lower lip was covered with a crust, when this was removed, a moist bleeding surface was seen. On each buccal mucosa, there were marginated superficial ulcerations the surfaces of which were covered with a yellowish membrane. There were no vesicles on the lips nor in the mouth.

In August, during the time lesions were in the mouth and on the skin, both eyes became inflamed. Examination showed intense infection of the palpebral and

bulbar conjunctiva. There was a distinct membrane on the tarsal conjunctiva of the lower lids and on the bulbar conjunctiva on the temporal side. Both upper lids were similarly affected. Examination by slit microscopy showed both corneas clear, there were no vesicles, the aqueous was clear, the iris intact, and the lens unaffected.

Infection of the conjunctiva gradually subsided, and the membrane on the conjunctiva in both eyes disappeared. In the latter part of September, there was a recurrence of conjunctival redness, membrane formation on upper and lower lids, and moderate swelling of the upper lid with free discharge. No vesicles were seen in either cornea.

The patient had no fever and no constitutional symptoms. Sulfadiazine was given internally, and sulfathiazole ointment was used in the eyes. Fowler's solution was administered by mouth in doses varying from 3 to 6 drops, three times daily. Repeated smallpox vaccinations were performed. A strict, saltless diet was instituted.

Ocular inflammation again subsided. The patient now presented only erosive areas on the inner surfaces of the lips and on the buccal mucosa.

Discussion. Dr. George S. Dublin said that it has been his good fortune to be able to see this case from its beginning. When first seen, there was noted a severe inflammation of the conjunctiva. A distinct membrane was present on the tarsal conjunctiva of the lids. This membrane, yellowish in color, appeared to be on the surface of the conjunctival epithelium and did not appear to involve the deeper layers. He had tried to remove part of the membrane but was unsuccessful. About two or three days later, a membrane appeared on the bulbar conjunctiva both temporally and nasally, paralleling the limbal border, in one eye extending to the outer canthus. In addition, there was a profuse ropy discharge

Dr. Klauder's earlier findings of vesicular formation in the skin together with a stomatitis pointed to a possible pemphigus. Mild lotions were prescribed, and the condition cleared to a remarkable degree in approximately 7 to 10 days, at which time the membrane completely disappeared in both eyes.

The patient volunteered the information that as soon as the eyes would become well, the mouth would break out into various sores. She was right. This condition in and about the mouth lasted four or five days, and then there was a recurrence of the ocular symptoms, and each time the membrane was more extensive than during the previous flare-up. Dr. Dublin said that he did not know how to treat the condition, since there seemed to be no adequate therapy. He had never seen a case with such an extensive membrane formation. There are other conditions simulating pemphigus; such as, erythema multiforme, dermatitis herpetiformis, and bullous syphilid. There are still other conditions which will produce membranes, both of the pseudo type and of the deep type of membranous conjunctivitis.

As we know, membranous conjunctivitis involves the deep portion of the epithelium or submucous portion and is invariably considered to be due to diphtheria. This patient was not acutely ill, nor was there any rise of temperature. As no diphtheria bacilli were found, the possibility of diphtheria was eliminated. A culture and smear were taken, but the bacteriologist was unable to identify the organism, stating that it was a very rare gram-positive bacillus.

The patient had two more flare-ups associated with new lesions in the mouth. No special treatment was ordered, since the condition would clear up under simple, bland medication. The patient, however,

received sulfanilamide, internally, in doses of 60 gr., daily, for approximately 10 days. The disappearance of the membranes, Dr. Dublin believed, was not due to the sulfanilamide, because they cleared up without it after previous attacks. When the patient was last seen all the lesions and membranes had entirely disappeared. It is significant that the cornea was at no time involved. There were no vesicles, nor any ulcer formation. The conjunctivas, both tarsal and bulbar, in spite of the dense membrane which was present, at no time showed any bleeding or ulcerated areas, or areas of adhesion. The vision at all times was 20/20 in each eye.

Pemphigus is a rare disease. It may assume an acute or chronic form. The acute form, occurring chiefly in butchers, is a virulent type, with marked constitutional symptoms, and frequently causes death. Chronic pemphigus is frequently called essential shrinkage of the conjunctiva. The cause is unknown, but it is associated with bullae in the skin and mucous membranes in various parts of the body. In the eye, vesicles are rarely seen in the conjunctiva. In their place, however, are small reddened areas, probably the end result of broken bullae. This condition is frequently incorrectly diagnosed or, at least, a proper diagnosis is not made until the late stages, when shrinkage of the conjunctiva takes place. The shrinkage of the conjunctiva is due to connective-tissue formation in the submucous portions of the conjunctiva. When this occurs, there is thickening of the conjunctiva with symblepharon formation and, eventually, ankyloblepharon.

Slitlamp examination in the late stages usually reveals perivascular thickening along the vascular network, together with a parchmentlike appearance of the conjunctiva. Vesicles in the cornea are seldom observed, but corneal changes do occur secondary to the conjunctival pathologic alteration. The diagnosis is made generally by a dermatologist on the finding of bullae and vesicles in the skin and in the mucous membranes of the body, especially the mouth, larynx, nose, and rectum. A pseudomembranous formation with a chronic type of conjunctivitis is sometimes seen. The membrane affects both the tarsal and bulbar conjunctivas, in contrast to the true pseudomembrane which affects only the tarsal conjunctiva.

In the case presented by Drs. Klauder and Cowan, vesicles were noted in the skin and in the mucous membrane of the mouth, with a history of numerous exacerbations. The eye findings consisted of a membranous conjunctivitis, with numerous flare-ups, and with complete disappearance of this membrane in 7 to 10 days. Although the conjunctiva has shown no permanent defect, in all probability there will be alterations of the conjunctiva. Time alone will confirm or disprove the diagnosis of pemphigus in the case.

Dr. William Lamotte said that, Dr. Klauder had stated that there is no laboratory test for pemphigus. There is reported in the literature, however, a so-called Macht test with which he was not familiar. He asked Dr. Klauder to describe this test and tell whether or not it had any value.

Dr. W. E. Fry suggested that another differential diagnosis may at times, have to be considered; namely, the difference between a vernal conjunctivitis and pemphigus. He mentioned this because of a case that had come under his observation about a year and one half earlier. The patient was seen by Dr. Klauder—a young woman who gave the history of having multiple lesions of the gums, which necessitated the removal of all of her teeth. Exactly what the lesions were was not known.

When this patient was first seen, the

ocular condition was that of papilloma formation over the palpebral conjunctiva. The symptom of which she complained was intense itching. This led to the belief that the condition was vernal conjunctivitis. Smears showed an enormous number of eosinophiles. There were numerous nodules. A biopsy specimen of one of them showed the tissue to be similar to that from cases clinically diagnosed as vernal conjunctivitis.

Dr. Klauder saw the patient, found evidence in the mucosa of previous lesions, and believed that the patient had pemphigus. The patient has since died. Except that it was not an accident, the exact cause of her death was not known. Presumably, however, Dr. Klauder's diagnosis of pemphigus is correct.

Dr. Warren S. Reese said that he would like to ask Dr. Klauder whether, in his experience, cases of ocular pemphigus usually show skin lesions?

Dr. Joseph V. Klauder answered Dr. Lamotte by stating that he did not think the Pels-Macht test an infallibe means of diagnosing pemphigus. False positive reactions are obtained, and the consensus of opinion is that it is unreliable.

He could not, offhand, give the percentage of patients with ocular pemphigus in which the disease exists without involvement of other mucous surfaces and without skin lesions It may occur without other lesions It may occur with mucous-membrane lesions, and it may occur with mucous-membrane lesions and skin lesions. In answer to Dr. Reese's question, however, he believes that only in the minority of patients is the disease confined to the conjunctiva. He estimated this minority to be about 25 percent. The literature is quoted to this effect in his paper with Dr. Cowan, "Ocular pemphigus and its relation to pemphigus of the skin and mucous membranes." (Amer. Jour. Ophth., 1942, v. 25, June, pp. 643-66.)

Herpes zoster ophthalmicus appearing after trauma

Dr. Joseph V. Klauder (by invitation) reported seven cases of herpes zoster, appearing after injury to the skin or to the cornea, inflicted in various ways and of variable degree. The disease appeared in the region of injury after an interval varying from about one to nine days. In some of the patients, symptoms of sensory disturbance or pain intervened between injury and outbreak of herpes zoster.

Of the seven patients, four had herpes zoster ophthalmicus. The injuries preceding appearance of herpes zoster ophthalmicus were: (1) foreign body in the cornea; (2) contact of the eye and forehead with sulphur dioxide; (3) bumping one side of head on a hard object without producing demonstrable injury to the skin, in two patients.

Review of the literature disclosed many reports of herpes zoster appearing in from 1 to 30 days after injury, at times trivial, to the skin or cornea. Herpes zoster had also been reported as appearing after lumbar puncture, after intramuscular injection of a medicament, after osteopathic manipulation of the spine, and after deep X-ray therapy in the region of a ganglion.

The etiologic mechanism of herpes zoster appearing after trauma was discussed. The incubation period of spontaneously occurring herpes zoster and of the disease when experimentally produced was discussed.

From considerations discussed, it was reasonable to assume that trauma may precipitate herpes zoster. The minimum degree of trauma and the interval between trauma and the appearance of herpes

zoster, in order to ascribe to trauma a causal role, cannot precisely be defined. From experimental evidence and clinical observation of spontaneously occurring zoster, the incubation period of the disease ranges from a few days to about two weeks. From the cases now reported of zoster appearing after trauma, and from a review of the literature, the intervals which predominate are one day to about three weeks.

Dr. Walter Lillie said that Dr. Klauder's presentation interested him, inasmuch as the cases he had reported concerning the use of smallpox vaccine in the treatment of herpes zoster ophthalmicus had no history of trauma. Since Dr. Klauder's cases show such a great variation in the time of onset after trauma (less than a day to six weeks), a real doubt can be raised as to the importance of the trauma. It is well known that it is not difficult to elicit trauma in almost any history of any type of condition. He recalled one case seen at the Mayo Clinic in which a patient, with blindness in one eye and a very small field of vision remaining in the other due to a pituitary tumor, received $2,500 when the court agreed that the visual loss resulted from a pair of pliers striking his forehead. It is agreed that herpes zoster is a virus disease, that belongs to the chickenpox family, having a definite incubation period of at least a week or more. This explains why many times herpes zoster and chickenpox can be found in the same family.

Dr. George F. J. Kelly said that, at the present time, he had under his care a patient with herpes zoster ophthalmicus. According to her statement, five days previous to the appearance of the lesion some hot lard had splashed on the involved area. He felt this to be coincidental and not causative.

Dr. Joseph V. Klauder replied that experiments made to ascertain if zoster is caused by a virus have given conflicting results. The opinion is stated by some that it has not been conclusively shown that zoster is caused by a virus and that the disease may represent a syndrome resulting from any process causing inflammation of the spinal ganglion. Others accept experimental evidence as valid proof of virus causation and regard the elementary bodies demonstrable in herpes zoster vesicles, particularly within the first 48 hours, as representing the specific virus of the disease. Proof of virus cause of zoster is not so readily demonstrated as is such proof of herpes simplex.

Surgical methods of treating paralysis of the superior oblique muscle

Dr. William E. Krewson, III, said that isolated, unilateral paralysis of the superior oblique is frequently encountered; bilateral involvement, occasionally. The pathologic physiology of ocular movements of such cases was reviewed.

The literature records relatively few cases treated surgically, and for these a great variety of procedures has been offered. At some time or other, most muscles attached to each eye have been used in one way or another. These include: (1) weakening of the homolateral superior rectus; (2) advancement of the homolateral inferior rectus; (3) advancement or transplantation of the homolateral external rectus; (4) weakening of the contralateral inferior rectus; (5) tenotomy or recession of the homolateral inferior oblique; (6) shortening of the contralateral superior rectus; (7) advancement of the paralytic superior oblique; (8) various combinations of two or more of these operations.

No standard sequence of corrective measures can be advocated for all cases. The plan of attack must be based on

measurements found in each individual case. If a choice is permitted, weakening of a depressor muscle is undesirable; strengthening of a depressor or weakening of an elevator is preferable. In bilateral cases, equalization and preservation of the remaining depressors is advisable.

Discussion. Dr. Francis Adler said that he would like to amplify one of the factors which Dr. Krewson mentioned, a factor which occasionally leads to an erroneous diagnosis of these cases. He believed that this condition was first pointed out by Chavasse, under the term "inhibitional palsy of the contralateral antagonist." It is seen in those cases in which fixation is customarily carried out by an eye with a paralyzed superior oblique. In these cases, there is not only a characteristic limitation of movement downward and to the side opposite the paralyzed superior oblique, but there is also limitation of movement of the nonparalyzed eye on looking up to the ipsilateral side. For example: In a case of paralysis of the left superior oblique, the left eye fails to move down when the eyes are turned down and to the right. In such a case, the right eye fails to move up when the eyes are turned up and to the right. This may easily be mistaken for a paralysis of the right superior rectus muscle. Dr. Adler believed that the explanation for this so-called inhibitional palsy is somewhat similar to the explanation of the vertical separation on looking down and to the right when the left superior oblique is paralyzed. The vertical separation on looking down to the right is due to two factors: (1) the weakness in the left superior oblique muscle; (2) the overaction of the right superior rectus. This overaction is due to the well-known law of Hering, that all voluntary movements are brought about by an equal innervation to the muscles of the two sides concerned in the movement. When we look down and to the right an equal innervation is sent to all of the muscles of the two sides which carry the eye in this direction. When one of these muscles is weak, the total amount of innervation is increased so as to bring about the full movement of this weak muscle, but the same amount of innervation is sent to the yoke muscle of the opposite side and so this muscle overacts.

On looking up and to the right, in a case of left superior oblique paralysis, when the left eye is fixating, the movement in this direction is made easier if the left superior oblique is paralyzed, because the left inferior oblique now has no resistance from its opponent. Less energy will be required therefore, to turn this eye out, up, and to the right; accordingly, less innervation is sent to the yoke muscle of the left inferior oblique—namely, the right superior rectus—and this eye fails to move up as far as the left.

Dr. Glen G. Gibson said that he had had experience with mistaken cases of superior-oblique palsy. One of the common types of cases in which the diagnosis may be incorrect are those simulating convergent strabismus. These were cases of palsy which started out primarily as a superior-oblique condition but, as time passed, they became concomitant, and it was almost impossible to differentiate them from cases of ordinary accommodative-convergent strabismus. In some of these, he at first failed to recognize their vertical origin and had operated as if they were cases of convergent squint, only to have them return with unsatisfactory results. Further study would then reveal that they were originally trochlear cases. A second operation produced gratifying results, because the surgical procedure recognized the primary pathologic involvement. Dr. Krewson believed that careful atten-

tion to the sensory correspondence was helpful in selecting the proper type and amount of surgical correction.

He illustrated the simplest operation by presenting a traumatic case of trochlear palsy of a year's duration in which there was 21 prism diopters of hyperphoria. This patient was subjected to a recession of the inferior rectus of the opposite eye. Following the operation, which consisted of a 2-mm. recession of the contralateral inferior rectus, there was no hyperphoria. In other words, the 21 prism diopters of hyperphoria had been reduced to zero by a minimal recession.

The important point in this case was not that it was an instance of very precise measurement of the amount of necessary surgical correction, but rather that a good surgical result was achieved because this patient originally had, and, until his accident, had always had, normal binocular vision. What was done was to put the eye somewhere near the normal place, and since the patient had normal binocular vision, the sensory mechanism helped to bring the eyes to the precise place where they were wanted.

If the case is long standing or congenital, a 2-mm. recession is not adequate for bringing about the desired result, particularly in cases that present a marked vertical tropia. In such cases it is necessary to do a recession of as much as 4 or 5 mm., about the maximum recession possible in the inferior rectus of the other eye. In some cases, especially those of long standing in adults, it is necessary to combine both the recession of the inferior rectus of one eye with a tenotomy of the inferior oblique of the other, or paralytic eye.

One other important point is the recognition of birth traumas and hereditary factors as a cause of trochlear paralysis. Recently two grandmothers, who have had that condition all their lives, were seen. They were grandmothers of two patients on whom operations for trochlear paralysis had been performed. This shows a definite hereditary factor for which the ophthalmologist should look.

Birth trauma is a common cause. It is fruitful to investigate these cases, particularly for the history of forceps delivery as a possible cause of original trochlear palsy. It is also important to recognize the degree of binocular vision that these patients have. If the condition has been present from birth, the individual never did have binocular vision except with an abnormal position of the head. A much more extensive surgical procedure is needed in these cases than in those of traumatic origin.

GEORGE F. J. KELLY,
Clerk

COLORADO OPHTHALMOLOGICAL SOCIETY

October 20, 1945

DR. WALTER OMHART, *president*

CHOROIDITIS TREATED BY PENICILLIN

DR. GEORGE H. STINE presented H. H. P., a white woman aged 35 years, who had first been seen about five weeks previously. She gave a history of previous attacks of choroiditis. At this time she had a large, atrophic, healed area with a fresh patch of exudate nearby, accompanied by paraphlebitis. The lesions resembled tuberculosis, but the tuberculin tests were negative. There was considerable peridental infection. The condition had improved following dental extractions, and foreign protein, atropine, and penicillin therapy.

RETINAL DETACHMENT, MYOPIA, MULTIPLE HOLES

DR. GEORGE H. STINE presented Mr.

W. C. K., aged 50 years, whom he had first seen on June 12, 1945. The patient complained of having had blurred vision for several weeks. This became much worse after an automobile drive over a rough road. Interesting features of the case were the high myopia and the presence of three holes. One near the macula was treated by galvanism. After treatment with perforating and nonperforating diathermy in the peripheral-tear areas, the retina was almost entirely reattached. A second operation, treating the region of the peripheral tears, was performed on September 6, 1945. At this time the retina was completely reattached with corrected vision of 20/200 in the right eye. Dr. Stine said that after retinal-detachment operations, there is an exaggeration of normal phenomenon; that the periphery is seen with more plus than the macula. This was illustrated in this case in that the macula was best seen with a minus 11 sphere whereas the peripheral-tear areas were seen with a plus two sphere.

Retinal detachment, multiple operations, posterior sclerotomy

Dr. George H. Stine presented Mrs. C. W. G., aged 67 years, who had been seen in 1931 and 1934 because of vitreous opacities. On June 18, 1934, a retinal detachment was found in the upper nasal quadrant of the left eye by Dr. Neeper. Pinhole glasses were prescribed, and the retina reattached by July 8, 1934. The detachment recurred on July 24th. It was larger than the previous one, but improved after bed rest and dental extractions. Surgery was performed in the upper nasal quadrant by Dr. Clifford Walker on August 13, 1934. The patient was operated on again by Dr. Stine on August 27, 1934. At this time a posterior sclerotomy was done in the lower nasal quadrant. A tear then developed in this area which Dr. Stine attributed to the posterior sclerotomy. A third operation was performed by Drs. Walker and Stine in the upper and lower nasal quadrants on September 17, 1934. The retina reattached 10 days later. At the time of presentation of the patient (11 years later), there were some drusenlike opacities in the macula, a few vitreous opacities, and a small posterior capsular cataract. Slit-lamp and plano-contact-lens examination showed marked forward contraction and shrinkage in each eye. The retina of the left eye was still in place, and the corrected vision was 20/30.

Osteoma of the orbit

Dr. K. H. Chapman presented G. R., a boy aged four years, who had had a swelling at the outer canthus just inside the lids since birth. When he was one year old, the swelling had been "opened" by an ophthalmologist, but the size had remained the same. On examination, Dr. Chapman found a narrow band of scar tissue in the conjunctiva extending from the outer posterior canthus for about 5 mm. Posteriorly and temporally to this was some fullness, but no definite mass could be palpated. The preoperative diagnosis was "accessory lacrimal gland which had become cystic."

While the child was under a general anesthetic for a tonsillectomy, a mass was dissected from the orbit just posterior to the lateral orbital margin, to which it was not connected. It was a firm, lobulated, freely movable, well-encapsulated mass about 2 by 1½ by 1 cm. in size and similar in appearance to a lacrimal gland. The pathologic diagnosis, however, was "osteoma." Dr. Chapman said that osteomas, invading the orbit from the sinuses, are relatively common, but that she had found no recent reports of one in the

temporal orbit unconnected with the orbital wall.

Microphthalmos, Harelip, and Cleft Palate

Dr. George H. Stine showed a kodachrome picture of an infant born with a major cranial deformity and other associated malformations including bilateral microphthalmia.

Discussion. Dr. William H. Crisp mentioned a case of microphthalmia associated with marked corectopia.

Another member said that he had recently seen a child with microphthalmia associated with a white congenital abnormality in the vitreous. In discussing the differential diagnosis, the question was asked whether any member present recalled ever having seen a case of retinoblastoma in one of these small eyes. No one remembered having seen such a case.

Acute Glaucoma, Paracentesis

Dr. William Bane reported the case of an elderly lady who had had an attack of acute glaucoma which had not responded to miotics. He had then performed a paracentesis, and the tension had immediately come down to normal and had remained so with a minimum of medication.

Discussion. Dr. William H. Crisp said that in some of these paracenteses and in Curran's operation we, in essence, had a small iridencleisis.

Cataract, Recurrent Iritis, and Deafness Secondary to Injury by Lightning

Dr. V. H. Brobeck and Capt. C. A. Fleischli presented G. W., a 22-year-old pilot of a B29 bomber, who had been struck by lightning four months previously, just as he had stepped out of his plane. He was unconscious for 36 hours but had made a complete recovery except for deafness in his right ear, diminished vision in both eyes, and recurring attacks of iritis. The poor vision was first noticed about a month after the accident, and examination revealed the cause to be capsular cataracts. Two months following the injury, the vision had been reduced to 20/50 in the right eye and 20/40 in the left. There had been no further loss of vision nor progress in the opacities since then. No foci of infection were found to account for the recurrent iritis. Dr. Brobeck said it was interesting to speculate on the manner in which the iritis was caused by the lightning. The iritis had responded to cycloplegics and foreign protein. An interesting feature of the case was the fact that the lightning had burned the amalgam fillings out of his teeth. The patient has an amnesia for events just prior to the injury.

Discussion. Dr. George H. Stine mentioned that in a family of three which was struck by lightning, two of the members developed cataracts and one was not affected.

Dr. R. W. Danielson said that the interval before developing cataracts was similar to that in dinitrophenol cataracts. In both cases the cataracts are probably secondary to the effect on the germinal epithelium of the lens.

Drs. W. A. Ohmart, J. W. Lamme, and E. R. Neeper also reported having seen cases of cataract secondary to injury by lightning.

Tumor on the Disc

Dr. Fritz Nelson presented J. E. W., a white man, aged 61 years, who said that about five years before, the vision of his left eye had deteriorated somewhat due to a fundus lesion of uncertain ori-

gin. The vision of the right eye had always been good. About 2½ years later, a little node began growing slowly below the left lower jaw bone. He was sent to the cancer clinic and received about 25 X-ray treatments to the left side of the naso-pharynx, whence the primary tumor had supposedly originated. The tumor below the jaw was not treated.

The patient was first seen by Dr. Nelson on January 26, 1945. At that time the tumor below the jaw was about the size of a hen's egg, very firm, and not attached to the skin and deeper layers. There was no dislocation nor exophthalmos (Hertel, 18 mm.) of either eye. The corrected vision of the right eye was 5/3 and of the left 5/6. Ophthalmoscopically, the right eye had a white prominence (about 2½D.) at the lower edge of the disc, which was partly covered by it. The formation resembled a bundle of medullated nerve fibers, but seemed to be globular in shape and more prominent than one would expect.

Dr. Nelson was suspicious of a metastatic tumor on the right optic disc. The probable general diagnosis was: "a slow-growing malignant tumor (sarcoma or mixed tumor) of the left, submaxillary salivary gland. The condition had not shown much change during the past nine months. Dr. Nelson planned a biopsy of the tumor below the left mandible.

Discussion. Drs. William M. Bane and George H. Stine and others believed the tumor was composed of medullated nerve fibers in spite of the elevation.

Malignant melanoma of iris and ciliary body

Dr. Fritz Nelson presented P. B., a white man aged 51 years. The patient was first examined in the fall of 1941, and neither eye showed any abnormality. In October, 1944, during a routine refraction, a small dark chocolate-brown fusiform tumor was found between the 7:30 and 8:30 positions, involving the root of the iris of the right eye. This tumor was about 3 mm. long and not quite 1 mm. wide. All functions of that eye, including the field of vision and visual acuity, were normal. Malignant melanoma of the ciliary body was suspected at that time, but no protrusion of a tumor from the ciliary body backward could be seen.

On April 4, 1945, the patient was reexamined. The tumor of the iris was of about the same size, but now protrusion from that region into the vitreous body could be seen ophthalmoscopically. The size of the tumor in the ciliary body was that of a very small pea. Because of the early stage, it was planned to destroy the tumor with a diathermic needle. The patient, following the advice of another ophthalmologist who told him that the eye was perfectly normal, refused treatment.

He was seen again on October 20, 1945, and a definite increase of the tumor could be seen ophthalmoscopically. The tumor was surrounded by a translucent or semiopaque zone, and the equator of the lens showed a small opacity probably caused by some influence from the tumor. Dr. Nelson thought that enucleation of that eye was now probably the only choice.

Discussion. Dr. George H. Stine advised a diagnostic iridectomy, examination of a frozen section and removal of the eye if the tissue showed malignancy.

Dr. R. W. Danielson said that the presence of the opacity in the lens was confusing. He recalled a case in his practice in which, with an undilated pupil an opacity of the periphery of the lens had ophthalmoscopically given the appearance of a tumor in the ciliary body.

Ralph Danielson,
Acting Secretary.

LOS ANGELES SOCIETY FOR OPHTHALMOLOGY AND OTOLARYNGOLOGY

SECTION ON OPHTHALMOLOGY

October 22, 1945

DR. K. C. BRANDENBURG, *presiding*

CLINICAL ASPECTS AND TREATMENT OF EXOPHTHALMOS FROM THE EXPERIMENTAL VIEWPOINT

DR. HARRY FRIEDGOOD reviewed the anatomic and physiologic aspects of experimental exophthalmos in lower mammals and correlated them with the clinical picture of exophthalmos in man. He stated that it was possible to produce exophthalmos in experimental animals by means of anterior-pituitary injections much more easily after removal of the thyroid gland than before. Dr. Friedgood said that of the various possible explanations for the mechanism of exophthalmos due to thyroid disease, it seemed that edema of the orbital tissues was the most likely.

It was concluded by Dr. Friedgood that the exophthalmos of this syndrome goes through two phases, the reversible and irreversible. He said the former was ordinarily encountered in exophthalmic goiter. The latter, he said, occasionally occurs as a postthyroidectomy complication.

The evidence, he pointed out, suggested that an exophthalmos-producing (ophthalmotropic) factor in the pituitary gland, distinct from the thyrotropic hormone, induces both types of exophthalmos. The use of the word ophthalmotropic, he said, does not imply that a specific chemical substance having the physiologic action is believed to exist as such in the pituitary gland. Dr. Friedgood said that because this factor is probably responsible for edema of the orbital tissues, it might be tied in with the important role which the pituitary and thyroid glands play in regulating water metabolism.

Although the irreversible or malignant type of exophthalmos cannot always be differentiated in advance from the benign or reversible type, certain clinical criteria aid in the diagnosis. Since edema of the orbit is probably an early pathologic change, one should regard with suspicion any preoperative chemosis, lacrimation, puffiness, or venous congestion of the lids or orbit. The development of hyperthyroidism during iodine therapy or the presence of thyrotropic hormones in the urine should put one on guard, according to Dr. Friedgood, as should a low basal-metabolism rate and increase in blood cholesterol.

He also stated that males with slight hyperthyroidism and considerable exophthalmos are peculiarly predisposed to the development of malignant exophthalmos following thyroidectomy. In his opinion operation should be avoided in suspicious cases or, if operation is necessary, the pre- and postoperative administration of desiccated thyroid may prevent the development of hypothyroidism, which is known to favor the development of malignant exophthalmos.

NEUROTICISM AMONG ANISEIKONIA PATIENTS

DR. K. C. BRANDENBURG, in collaboration with his associate, Dr. Hazel Wentworth, made a preliminary report on a study of the neurotic factor among aniseikonia patients (utilizing the Harrower-Erickson modification of the Rorschach test). They had divided a series of 50 patients into three groups and scored them according to their percentage of poor

answers on the Harrower-Erickson multiple-choice test as follows:

	Number Cases	*Median Score* percent*	*Average Score* percent*
Group I			
No symptoms—no aniseikonic test	7	6.5	12
Group II			
Symptoms—1% or more aniseikonia			
A. Marked or complete relief	23	11	15
B. Partial relief	9	23	21
C. No, or only slight	10	40	39
Group III			
Symptoms—No aniseikonia or less than 1%	11	20	27

* Scoring of H-E Rorschach: 0 percent—no poor answers; 100 percent—all poor answers; under 40 percent—normal; 40 to 50 percent—borderline; over 50 percent—disturbed personality.

Dr. Brandenburg called attention to the limited number of cases tested in each group, rendering the reliability of the results somewhat questionable. He also pointed out that the averages for all groups fell within what was considered the normal range of bad answers.

There was, however, a definitely greater average of bad answers among aniseikonia patients who received no, or only slight, relief from their correction (39 percent) than among those who received complete relief (15 percent), or only partial relief (21 percent). Whether the percentage of bad answers within the normal range could be considered a criterion of a degree of neuroticism had not been established experimentally as far as the essayists were aware. Dr. Brandenburg reported that the figures seemed, however, to corroborate the clinical impression that when aniseikonia exists in an individual who does not manifest marked neurotic tendencies, iseikonic lenses are more likely to give lasting relief than in cases wherein the neurotic factor is of greater importance. He stated that the study would continue.

Psychologic problems of impending blindness

Mr. J. Milton Johnson of the Braille Institute stressed the psychologic importance of acquainting persons with impending blindness with the many activities, useful and diverting, which are available to the blind. He thought it to be desirable that they learn these things from someone who was, or had been, blind and could therefore understand the hopes and fears of one whose vision was failing or had failed. He described the various activities of the Braille Institute of America and asked the coöperation of the eye specialists in making these contacts possible.

C. H. Albaugh,
Reporter.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*
55 East Washington Street, Chicago 2
WILLIAM H. CRISP, *Consulting Editor*
530 Metropolitan Building, Denver 2
LAWRENCE T. POST, *Consulting Editor*
640 South Kingshighway, Saint Louis 10
WILLIAM L. BENEDICT
The Mayo Clinic, Rochester, Minnesota
FREDERICK C. CORDES
384 Post Street, San Francisco 8
SIR STEWART DUKE-ELDER
63 Harley Street, London, W.1
EDWIN B. DUNPHY
243 Charles St., Boston 14
HARRY S. GRADLE
58 East Washington Street, Chicago 2
F. HERBERT HAESSLER
324 East Wisconsin Avenue, Milwaukee 2
PARKER HEATH
1553 Woodward Avenue, Detroit 26
S. RODMAN IRVINE
9730 Wilshire Boulevard, Beverly Hills, California
DONALD J. LYLE
904 Carew Tower, Cincinnati 2
IDA MANN
The Eye Hospital, Oxford, England
ALGERNON B. REESE
73 East Seventy-first Street, New York 21
PHILLIPS THYGESON
524 Sainte Claire Building, San Jose, California
M. URIBE TRONCOSO
500 West End Avenue, New York 24
F. E. WOODRUFF
824 Metropolitan Building, Saint Louis 3
ALAN C. WOODS
Johns Hopkins Hospital, Baltimore 5

KATHERINE FERGUSON CHALKLEY, *Manuscript Editor*,
Lake Geneva, Wisconsin

Directors: LAWRENCE T. POST, President; WILLIAM L. BENEDICT, Vice-President; DONALD J. LYLE, Secretary and Treasurer; WILLIAM H. CRISP, HARRY S. GRADLE, DERRICK VAIL.

Address original papers, other scientific communications including correspondence, also books for review to *Dr. Derrick Vail, 55 East Washington Street, Chicago 2, Illinois;* Society Proceedings to *Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Manuscripts should be *original copies,* typed in *double space,* with wide margins.

Exchange copies of medical journals should be sent to *Dr. F. Herbert Haessler, 324 E. Wisconsin Avenue, Milwaukee 2, Wisconsin.*

Subscriptions, application for single copies, notices of changes of address, and communications with reference to advertising should be addressed to the *Manager of Subscriptions and Advertising, 837 Carew Tower, Cincinnati 2, Ohio.* Copy of advertisements must be sent to the manager by the fifteenth of the month preceding its appearance.

Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Twenty-five reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Publishing Company, 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

FEDERAL INVESTIGATION OF REBATING

In a Saint Louis newspaper of July 24th appeared this headline: "Anti-Trust Suits Charge Rebating to Eye Doctors" and, in a subheading, "Civil Actions name Seven Concerns, about 5,000 Individuals, and ask for Injunctions."

I quote the first paragraph of the article: "The Department of Justice today filed two civil suits in Federal Court charging optical wholesalers and approximately 5,000 leading eye doctors throughout the country with violating anti-trust statutes." Thirty eye doctors were named in "a representative capacity" representing 3,000 doctors who are accused of receiving rebates regularly from one company. Another company is accused of rebating through its subsidiaries to another 3,000 eye doctors. Allowing for some overlapping, probably 5,000 eye doctors are involved directly or indirectly in the suit. There are about 7,500 ophthalmologists in the nation. Approximately two thirds are, therefore, accused.

Since writing these introductory paragraphs, there have appeared copies of the indictments in the Journal of the American Medical Association and an editorial in the same issue which merely stated the resolutions passed previously by the Ophthalmic Section and the action of the House of Delegates on these resolutions.

In other newspapers, in addition to the names of the representatives in the two indictments, there apparently appeared the names with the amounts allegedly rebated to some of the ophthalmologists.

The writer has always strongly contended that it is ethically wrong to take a hidden fee from a patient and that an ophthalmologist should not profit in any direct financial way from the sale of lenses or their appurtenances. This is the rule of ethics of the American Medical Association, but it has admittedly been disregarded by many members of its official Eye Section.

In discussions of the matter, one often encounters the comment "Granted that the practice is current, surely you don't want the public to lose confidence in the eye doctor by letting people know about it." The answer is that no one should have the public confidence if he does not deserve it. One usually then hears the statement that those in the eye specialty are not alone guilty, that rebates are taken on orthopedic appliances, ear phones, drugs, and other items, so why should ophthalmologists be singled out for punishment. Obviously, everyone who engages in such practices should be called to account, but unethical conduct in one person is not a good excuse for it in another, and it is the ophthalmologists' misfortune that they have been selected for action.

What a perfect opportunity this well-known practice has given to those whom ophthalmologists have attacked on ethical and moral grounds to say "Look who are calling the kettle black."

Unfortunately, we could not or, at any rate, would not handle this matter within our own profession so now the Federal Government has taken the task over.

Whether doctors who accept rebates are legally liable or not is not for the writer to say. If the doctor has failed to show in his income tax report any money received, that is another story and no lawyer is needed to answer that question, and the eye physician would better engage a good one to defend him. The rebater has surely had the transactions on his books and, undoubtedly, the Government has already secured these books containing the lists of names and amounts rebated.

It would probably be desirable for the profession to know everything about these matters. The writer guesses that, unfortunately, there are some in very high places whose names are on these lists. Whether it would have a salutary effect or not for everyone to know the names of those who engage in these doubtful practices is a moot question. Frankly, the writer would not enjoy seeing them exposed before their friends and patients. Actually, some of this may never happen but the indictments bring up once more this disagreeable problem that has thus far baffled all who have tried to eliminate it. Medical disciplinary action in this matter must of necessity fall upon the American Medical Association because the Ophthalmic Section has no authority to handle it. By the nature of the Constitution of the American Medical Association, ultimate discretion in regard to ethics rests with the county medical societies, and the Ethics Committee of the House of Delegates, if it takes any action at all, will probably refer the matter to these hundreds of county organizations, possibly after a few generalities on the subject. It is not necessary to comment on the complete lack of action that

would be taken by most of the local medical societies.

But is not there anything that can be done to eliminate these unwholesome practices that cast opprobrium on all physicians and furnish good grounds for the Government's lack of faith in the ability of the medical profession to act in the best interest of the public? The Government apparently is now fully aware of the existence of rebating and believes it is illegal and harmful to its citizens. We must agree that it contributes to increase the cost of glasses and that in itself is detrimental to the general welfare. Wholesalers and retailers alike must surely want the practice stopped. It does them no good and is financially harmful.

The writer suggests that the Executive Committee of the Section on Ophthalmology of the American Medical Association appoint a committee to confer with Government agents, wholesalers of optical goods, and representative retailers for a frank discussion and an effort to adopt a course to bring about a termination of this abuse. The Government may frighten some out of rebating and receiving rebates, but the coöperation of all of those interested in the matter might prove even more effective than the governmental warning and fining of a few individuals selected to be the scapegoats for other possible offenders.

National and local ophthalmic societies and The American Board of Ophthalmology have no police powers and should not have, their functions are other than this, but a stronger attitude by them on "kickbacks" and rebates would be helpful in stamping out this pernicious practice and would more definitely indicate to the young men entering our specialty our wholehearted disapproval of it.

Lawrence T. Post.

A STANDARDIZED CURRICULUM

The need for more graduate courses in ophthalmology is as acute as it is obvious. The number of applicants for such training is tremendous. The reason for the large number is not difficult to find. Many physicians, while serving in the Armed Forces, were brought into contact with ophthalmology, usually under the guidance of a well-trained, older man. The result is that they would like to choose it for their own specialty.

The interest thus stimulated is no idle one, no passing fancy, but rather it is deep and sincere. The ultimate goal of the large majority is certification by the American Board of Ophthalmology. This is gratifying and is as it should be. One has but to interview these men to be convinced of their sincerity and singleness of purpose.

The available graduate courses in ophthalmology are few. These few are probably satisfactory, but no doubt there is room for improvement. Each course has its strong points, depending upon the interests of its faculty; similarly, each course has its weak points and for the same reason. It behooves us to take stock of our courses, to examine critically their curricula. How well are they preparing candidates for the examination of the American Board of Ophthalmology and, what is more important, for the clinical practice of good, sound ophthalmology? It would be wise to look for weak spots, for they are surely there.

It would be wiser still to have a "stranger" or even a board of strangers examine our curricula than to do it ourselves. It is objective, constructive criticism that is desired. The fresher viewpoint of an outsider would be invaluable.

Such a board might be formed under the auspices of the American Board of Ophthalmology or by any one or all of the

three national ophthalmic organizations. Its function would be to analyze the curricula of available courses with the view of taking the best from each and developing a standardized program for such courses. Just as the American Medical Association inspects medical schools in this country, so should such a board inspect graduate courses in ophthalmology. Our courses are probably good, but they could be made better.

One value of such a standardized curriculum, bearing the Board's stamp of approval, would be that it could be made available to many institutions to serve as a guide for the establishment of more courses. It seems probable that many large institutions have a wealth of clinical material at hand and also a faculty. All that they need is a blueprint in the form of a detailed, standardized, approved curriculum and a little encouragement.

At the moment, those conducting the available graduate courses in ophthalmology are on their toes. They should be kept that way. And other such courses should be initiated. The demand of large numbers of applicants makes it imperative.

Richard G. Scobee.

CENTENARY OF ANESTHESIA

On October 16, 1846, Morton dramatically introduced general anesthesia to the operating theater. The eminent and humanitarian surgeon, John C. Warren, with a courage reminiscent of Joseph Warren, his uncle, who fell at Bunker Hill, risked his great reputation in this hazardous experiment. The patient was Gilbert Abbott, a painter and single.

As now the atom holds the spotlight, so, in the early 19th century, gases and vapors dominated scientific attention. Beddoes became mystically inspired by their possible therapeutic value and, in his Pneumatic Institute, Davy, in 1800, and Faraday, in 1818, discovered the insensibility produced by nitrous oxide and ether, respectively. These observations excited a minimum of attention. Even as later as 1831, Velpeau pontifically dismissed the hope of ever operating without pain. By 1839, however, the Materia Medica mentioned that ether could produce stupefaction. Then Long, at the age of 26, Morton at 27, and Wells at 29—obscure young men ignorant of Velpeau's dictum—demonstrated its fallacy. The concept of "anesthesia" now had a footing, and Oliver Wendell Holmes supplied the word.

But not all were convinced. Wrote Thomas E. Bond of Baltimore in the Boston Medical and Surgical Journal of December 15, 1846: "What your correspondents are pleased to call 'producing insensibility' is, in fact, making people 'dead drunk.' . . . Now, doctor, if we are to induce insensibility by this class of means, I very much prefer whiskey-punch to ether, because it is more certain and more permanent in its effects. It is less dangerous, and, lastly, it will be easier to persuade patients to take it."

Before the advent of local anesthesia in 1884, eye surgeons faced the choice of operating under general anesthesia or none and not infrequently decided that the advantages were with the latter alternative. William Mackenzie, in 1854, advocated general anesthesia for children, and for discussion on timid adults. But he continued: "In extraction I have not ventured to use it, being afraid lest the vomiting which is apt to follow might cause rupture of the internal structures of the eye. I have read, however, from others who have used it in extraction, a very favorable account of the complete stillness of the eye which it affords." Henry S. Schell of Wills Eye Hospital, in 1881, expressed the same viewpoint: "If the

patient is of steady nerve, and can be relied on to obey orders promptly, it will be more satisfactory to both parties to dispense with ether. . . . The pain of the incision is not very great, and slight pauses, with closed lids, may be allowed between the steps of the operation." But B. J. Jeffries of the Massachusetts Charitable Eye and Ear Infirmary, in 1871, declared otherwise: "In these days of ether and chloroform, one or the other is always administered, so that the patient suffers no pain, and after the operation is often unable to say which eye was operated on."

Intravenous anesthesia was widely used during the late war in the expeditious surgery of eye casualties only just evacuated from battle, and it proved a priceless boon to the tense, exhausted warriors. Because of its effectiveness and relative simplicity, this latest development of general anesthesia certainly merits wider acceptance for the eye surgery of everyday civilian practice.

James E. Lebensohn.

WETTING AGENTS AND DETERGENTS

References to the use of wetting agents and detergents in ophthalmic drugs became fairly common in 1941 and 1942. There is experimental evidence that important and desirable effects are sometimes produced by addition of specific surface-active agents to certain therapeutic preparations. These effects are: (1) increased solubility permitting higher concentration of therapeutic drugs to come into contact with the eye; (2) increased penetration into the cornea and other ocular tissues; (3) longer persistence of the therapeutic substance in the conjunctival sac in spite of dilution of the drug with tears.

The second of these effects is the one for which the most experimental data have been presented, but the *modus operandi* is not explained to the satisfaction of the average clinical ophthalmologist. The benefit of using wetting agents or detergents is based on theoretical assumptions as to their action which, to the practical man, is discounted by certain evidence that the desired effects may be produced mainly by damage to the corneal epithelium.

The purpose of this editorial is to discuss the theoretical considerations involved in the use of wetting agents; to attempt to clarify "lowering of surface tension," which is the explanation most frequently encountered; and to review, briefly, evidence of damage to the corneal epithelium.

Because many of the recently introduced synthetic detergents combine properties of wetting agents and detergents in a single molecule, there has been a tendency to neglect any consideration as to whether the specific agent is chosen for its wetting power or detergency. Although knowledge in the realm of wetting agents and detergents is still rather limited, some consideration of the distinctive properties of each might help us to predict the type needed for a specific purpose.

Most detergents are wetting agents, but the very best wetters are not always detergents. A detergent must have wetting properties so that the soil or contamination on the surface will be completely wetted, that is, covered with fluid, whereupon the distinctive property of the detergent comes into play. The detergent lowers interfacial tension between soil and solution and lifts globules of soil off the surface, keeping them in solution or suspension so that they are not redeposited. The lifting of the particles off the surface into the solution is the distinctive action of the detergent. This may be accomplished through surface-action effects, influence on solubility, and by frothing or agitation. Usually, it is accomplished by a

combination of two or more of these factors.

The cleaning of a surface by a detergent can be readily appreciated as important in bringing therapeutic agents into truer contact with the absorbing surface, as, in the case of the cornea, by removal of exudate and detritus from the corneal surface, allowing uniform distribution of the solution over the entire surface. We have all observed how dew occurs as spherical drops of water on the surface of a leaf. Between the drops there is an exposed dry surface. The exposed surface will always have on it dust, insecticide powder, or other finely divided substances of some sort. In a heavy shower, all the dust is washed off, and the remaining water no longer forms drops but wets the whole leaf and forms a thin layer over the whole surface.

A wetting agent, like a detergent, lowers interfacial tension so that there is wetting with spreading of the fluid over the surface, but it does not necessarily clean the surface. It may leave the contaminating particles still adherent to or, in spreading, wash them onto another part of the surface.

How does a wetting agent induce a solution to spread over and penetrate into a surface?

We all know the theory that the molecules in any substance attract each other by electrical forces. We readily see that the attraction forces in the interior of a mass of liquid will be balanced in all directions but that, at the surface, there will be an uneven distribution of forces inward. The cohesive forces holding the substance together are not balanced at the surface, and there is a pull toward the interior exerted on the surface layers. To break this surface, it is necessary to do work, to exert force. Since this surface force is uniform, due to the averaging effect of the very large number of molecules per unit of surface area, and since it tends to produce a surface with the smallest possible area, there results a spherical shape in any drop of liquid free from the effect of gravitational forces. The work required to overcome this surface force is called the surface tension.

Now, if there are two constituents of a solution and the molecules of one have a higher attractive field of force around them than the molecules of the other, and, if the molecules of higher attraction are present at the surface, a liquid with a comparatively high surface tension results. Contrariwise, if the molecules with the smaller fields of force are at the surface, the surface tension is smaller. Since the molecules are free to move, the liquid will always tend to cover itself with the molecules of the constituent possessing the smallest field of force. Consequently, we choose, as a wetting agent, a substance with low cohesional forces, and we cover the matrix fluid with a film of the wetting agent. Thus, we modify the surface tension of the fluid, lowering it so that it has less tendency to conglomerate and more tendency to spread.

If the attraction of the matrix liquid for molecules of the added substance is greater than their cohesive forces, the added liquid, or solid, will spread and, in so doing, the substance forms a film over the matrix liquid. If the cohesive forces are sufficiently weak, the added substance will spread uniformly over the surface. The action of a surface-active agent in wetting is, therefore, due to the repulsive forces which occur between molecules of the agent collected as a film on the surface of the main body of fluid. This repulsion resists the concentrating effect of the contraction forces existing on the surface layer of the main body of fluid. It is a repulsion that not only counteracts these contraction forces but also acts to push the matrix fluid into corners and over sur-

faces that would not ordinarily be wetted by this fluid. The surface-active effect depends on the molecules remaining as a film on the surface.

Langmuir, in 1917, introduced the ideas, still accepted, concerning the orientation of the molecule in these surface films. These ideas are discussed by Roth (Amer. Jour. Ophth., 1946, v. 29, p. 717). To illustrate, for one group of substances: Molecules of fatty acids and alcohols contain the water-soluble, hydrophilic groups (OH and COOH) and water-insoluble, hydrophobic groups. The hydrophilic groups tend to solubilize the molecule. In the case of shorter chain molecules, as methyl and ethyl alcohols and acetic acid, these groups are sufficiently hydrophilic, unbalanced by hydrophobic groups, to solubilize the entire molecule and, therefore, leave no surface effect since the alcohol or acid is readily diffused beneath the surface of the matrix fluid. With an increase in length of the chain, the solubility decreases, and there is a balance of hydrophilic and hydrophobic groups tending to produce a molecular surface film. As we come to the very-long-chain fatty acids, the solubilizing effect is so retarded that there is no surface film, no spreading, and no effective reduction of surface tension.

If the molecule contains two hydrophilic groups attached to opposite ends, the strong water attraction holds the molecule flat on the surface, resulting in a type of film in which the hydrophobic portions of the adjacent molecules are not in sufficiently close proximity to permit the repulsive forces to become important.

It is apparent that, if a substance is to reduce surface tension effectively, it must have a water-soluble, hydrophilic portion (when water is the matrix fluid, otherwise the solubility must be for whatever matrix liquid is used); and it must also have a water-insoluble, hydrophobic portion in its molecule. A proper balance keeps the agent at the surface; yet, there should be enough attraction to the water to cause spreading of the agent and, with it, spreading of the water.

To illustrate what we mean by balance between end-groups, we might think of the surface-active molecules behaving as would nails stuck into corks in such a way that the nails stand up as masts held at the surface of the water by the corks. Hydrophobic portions of the molecules would be the nail heads; hydrophilic portions, the nail in the cork.

The simplest case of wetting is the result of the spreading action we have tried to visualize as caused by the repulsion between molecules of surface-active agents and the subsequent overcoming of the tendency of the liquid itself to present a minimum surface.

The effect of surface-active agents on surface tension is influenced by the presence of water-soluble salts, such as sodium chloride and sodium sulfate. The salts affect the hydrophilic nature of the water-soluble portion making it less water soluble. For surface-active agents having considerable solubility, decreased water solubility may make an agent more effective in reducing surface tension, and vice versa. The properties of a surface-active agent, such as stability and surface tension, depend largely, therefore, on the nature of the end groups of the surface-active agent and the balance achieved between them. The surface-tension value given for a particular liquid by a surface-active agent is a function of the cohesional forces acting between the molecules of the film. Other things being equal, lowered cohesional forces are desired.

Coupled with low surface-tension factors in wetting are such properties as solubility, substantivity, and the condition of the surfaces. Of two liquids, the one with lower surface tension will spread

more rapidly over a clean surface, other conditions, such as viscosity and volatility, being equal. Or, at equilibrium, the liquid with lower surface tension will cover the greatest area, the qualities involved being equal, regardless of viscosity. As we all know, two drops of clean mercury on a clean plate readily join into a single drop; two less pure drops on a dusty plate become a single drop with difficulty.

Many wetting agents, soap being the most familiar example, are rendered insoluble and ineffective in the presence of heavy metal ions, with a change in hydrogen ion concentration, or with a change in salt concentration. Such influences by the varied constituents of a therapeutic preparation must be considered when a special surface-active agent is to be added.

Another factor which must be considered is that the attraction between the surface-active agent and the surface may not be chemical but physical, induced by electrical charges. This property is said to be substantive. These considerations help us visualize, to some extent, how the addition of a surface-active agent may bring about a closer contact of a therapeutic drug with the surface to be covered. Sometimes, this is accomplished by cleaning the absorbing surface; sometimes, by solubility effects; and sometimes, by increased spreading of a film over a surface.

A consideration of the increased penetration of therapeutically active substances through the cornea leads us to a consideration of the rise of a fluid in a capillary tube. Defining surface tension (γ) as the force in dynes required to extend the surface of a liquid along a line one centimeter in length, we have the formula:

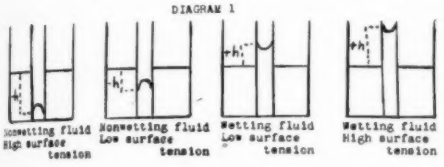
$$\gamma = \frac{h\,r\,d\,g}{2}.$$

Where h is the height of rise of liquid in the capillary in cm., r is the radius of the capillary in cm., d is the density of the fluid in g/ml, and g is gravitational acceleration, 980 dynes/cm^2. We see that, the higher the surface tension, the greater the penetration into capillary pores in the corneal epithelium, unless the value of h is negative. In general, h is positive; that is, when liquid touches the walls of a capillary or pore, the attraction of the molecules of the wall for the molecules of liquid is greater than the attraction of the molecules of liquid for one another. The liquid, therefore, wets the wall of the tube and creeps up the wall to the height calculated as h in the above equation. Obviously, the higher the surface tension, the higher the liquid ascends in the capillary.

If the attraction of the molecules of the wall of a tube for neighboring molecules of liquid is less than the attraction of the liquid molecules for one another (as in the system mercury glass), the liquid will fail to wet the wall and will be depressed rather than elevated, giving a negative value of h. By making a previously non-wetting fluid wet the wall of the capillary, the sign of h may be reversed. For instance, assuming that a membrane has pores of capillary dimensions lined with a fatty material which is not wetted by water, the capillary rise of water in such a pore will be negative. Surface tension, as usually understood in biologic papers, is surface-tension at such an oil-water interface. This surface tension is markedly reduced by such agents as aerosol. If, then, by addition of a wetting agent, as one of the aerosols, sulfosuccinate acid esters, the water can be made to wet the walls of the pore, the rise will become positive. If the height of the pore is less than the height of the capillary rise, the fluid will freely penetrate the membrane.

Assuming that our problem is to stimulate the flow of fluid through a porous membrane, the addition of a wetting agent helps us to accomplish this purpose best if it brings about wetting of the pores with the least amount of coincident lowering of surface tension. A consideration of the paradoxical mechanism of the action of a wetting agent in the penetration of fluid through a capillary pore may help in the choice of a specific wetting agent capable of giving the greatest desired effect.

The following simple diagrams illustrate this idea.



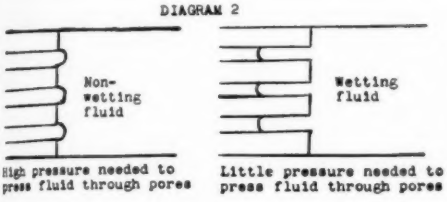


DIAGRAM 2
Non-wetting fluid
Wetting fluid
High pressure needed to press fluid through pores
Little pressure needed to press fluid through pores

A complete discussion of factors influencing permeability through a semipermeable membrane would bring into consideration the mechanism of anomalous osmosis, with the complicated concept of a membrane (an aggregate of a number of pores of different sizes), the summation of whose properties is measured by investigation not only of permeability but of diffusion rates, conductivity, dynamic membrane potentials, and so forth. We do not intend to discuss semipermeable membranes here, only to emphasize the effectivity of wetting as one factor in the theoretical deviation of rate of flow of fluid through a membrane.

When the effectivity of an opthalmic drug is increased by the addition of a wetting agent, this phenomenon can, theoretically, be attributed to the cleansing action of the wetting agent on the absorbing surface; to the increased solubility of the drug in the epithelium; to the increase of the flow of fluid through capillary pores by bringing about wetting of the pores and, thereby, overcoming the epithelial barrier; or, finally, to the elimination of the epithelial barrier by damage to the corneal epithelium.

Consideration of evidence that the cause of increased corneal permeability in the presence of wetting agents may possibly depend on damage to corneal epithelium is now in order.

Detergents are known to be good protein-denaturing agents. Many are fairly good antiseptics and bacteriostatics. Zephiran has been shown to have a bactericidal effect on Staphylococcus aureus.

The addition of minute amounts of a variety of wetting agents and detergents is known to alter certain proteins, poisoning such enzymes as trypsin and lipase, inhibiting the peptic activity of gastric contents, and lowering the biologic activity of lactogenic hormones. These facts make us wonder what harmful results such chemicals may have on the cholinesterase and the lysozym of tears. We ponder the potentialities inherent in inhibiting the activity of these enzymes and others related to the metabolism of the eye. Tears and meibomian secretion, themselves, have constituents which effect the surface tension at the tears-cornea interface, and tears and meibomian secretion, therefore, affect the permeability of the cornea. Tears are a natural wetting agent, and their antiseptic properties, attributable to lysozym, are of considerable importance. We hesitate to neutralize these properties.

Swan (Amer. Jour. Ophth., 1944, v. 27, p. 1118) showed that minute con-

centrations of detergents, especially zephiran chloride, as low as 0.025 percent, resulted in a violent reaction in the rabbit eye when injected into the anterior chamber. He reported development of conjunctival edema and desquamation when a single drop of 0.1-percent, zephiran-chloride solution was applied to the human cul-de-sac. Repeated instillations of zephiran chloride in concentrations as low as 0.03 percent produced conjunctival and corneal changes which were reparable when application of the drug was stopped. Leopold (Arch. of Ophth., 1945, v. 34, p. 99) reported conjunctival and corneal damage from repeated applications of detergent solutions, zephiran chloride producing corneal damage in concentrations as low as 0.1 percent. Repeated applications of solutions containing 0.5 percent of each detergent tested definitely retarded regeneration of corneal epithelium, and a 0.1-percent solution slightly retarded regeneration. Alvaro (Arch. of Ophth., 1943, v. 29, p. 615) mentioned increased penetration of sulfonamide compounds into the eye after first using one drop of sodium dioctylsulfosuccinate. This wetting agent is commercially known as decresol OT, and one drop would be very likely to produce corneal damage.

Ginsburg and Robson in the British Journal of Ophthalmology for April, 1945, offer what seem to be the most specious conclusions to date: "The penetration of sodium sulphacetamide into ocular tissues was studied in living rabbits and in isolated ocular tissues. Application of the drug with a wetting agent, Duponal ME dry (derived from Lauryl alcohol), increased penetration of sodium sulphacetamide into and through the cornea. The removal of corneal epithelium caused great increase in penetration of sodium sulphacetamide into and through the cornea; therefore, the epithelium was acting as a barrier to passage of the drug. The wetting agent did not increase the passage into the denuded cornea (epithelium removed), and so the wetting agent acts by overcoming the epithelial barrier."

They did not say whether the epithelial barrier was overcome by penetration through the barrier because of surface-active effects by the wetting agent, or by damage to the epithelium by the agent. They did suggest that the addition of a wetting agent to sodium sulphacetamide was of value in infections of the cornea and iris. It not only increased the concentration in the anterior ocular tissues but prolonged the period of effective chemotherapeutic concentration.

In conclusion, we might emphasize the advice, given by Swan and by Leopold, that the use of detergents should be considered with a knowledge of their possible toxic properties. In other words, the benefits to be obtained by their use must be weighed against the possibility of damage to ocular tissues in each case for which they are prescribed. Use of detergents in cases where there are abrasions of the corneal surface, might cause regeneration of the corneal epithelium to be unduly retarded. Their use when there are perforations of the eyeball, by injury or operation, might allow sufficient detergent to enter the anterior chamber to produce untoward reaction. These and other possibilities must always be considered.

On the other hand, the seriousness of the condition for which medication is prescribed, particularly the extent of any infectious process, may be so great as to justify any measures that might overcome the infection. The cases in which applications of preparations containing detergents are recommended for use over a prolonged period must be examined at routine intervals to determine whether

any local damage is discernible while it is still superficial.

In brief, we find by theoretical consideration and by actual experimental evidence that certain benefits are attributable to the use of wetting agents and detergents in ophthalmic drugs, but we are left with a realization of the possible toxic effects and a challenge to find better wetting agents with less toxic properties.

S. Rodman Irvine.

OBITUARY

GRADY EDWARD CLAY

1889-1946

Dr. Grady Edward Clay was born November 12, 1889, in the village of Walnut Grove, Walton County, Georgia. He died following a heart attack on July 11, 1946. He was the only child of Augustus C. Clay and Lizzie Chupp Clay. He retired during his last illness to his plantation at Walnut Grove.

Dr. Clay's preparatory education was received in Monroe, Georgia, and Emory College, where he was graduated in 1910. He received his medical degree from the University of Michigan in 1914 and was resident in ophthalmology for the next three years under the able Dr. Walter R. Parker.

He returned to Georgia in 1917 to begin private practice and at that time became an instructor in the eye department of Emory University Medical School. He entered the Army in 1918, serving 18 months overseas with the A.E.F. in France as ophthalmologist in a base hospital. He returned in 1919 and was discharged with the rank of captain. Upon resuming private practice and his association with the department of ophthalmology of Emory University, he rapidly demonstrated his ability and interest in teaching.

Dr. Clay was a member of the Fulton County Medical Society, the Atlanta Eye, Ear, Nose, and Throat Society, the American Medical Association, Southern Medical Association, Southeastern Surgical Congress, Academy of Ophthalmology and Otolaryngology, and the American

Ophthalmological Society. He served as president and member of the board of trustees of Fulton County Medical Society; chairman of the Ophthalmological Section, Southern Medical Association in 1936; associate editor of the American Journal of Ophthalmology; member of the Council of the American Academy of Ophthalmology; vice-president of the Southeastern Surgical Congress, 1939; and member of the American Board of Ophthalmology. For two terms, from 1936 to 1938, he was president of the Emory University Alumni Association, and served on the university Board of Trustees. He was chairman of the alumni committee that sponsored construction of the present Phi Delta Theta house at Emory University and was elected to Omicron Delta Kappa, national honorary society, for "outstanding service" to the

university. He was a member of the general advisory committee of the National Society for the Prevention of Blindness; and was chairman of the advisory committee on ophthalmology for the Georgia State Department of Public Welfare from 1941 to 1944.

In 1939, he was made chief of the department of ophthalmology and a full professor in 1943. He obtained, through his patients and influential friends, substantial financial aid for the Eye Department and had established a laboratory for ocular pathology and bacteriology.

Grady Clay possessed a forceful personality and was a splendid organizer. In his lectures, he was most instructive to students and staff alike. His great interests were in medical- and neuro-ophthalmology. One of his pet interests was the vascular changes in the retina, and he had striven for years to simplify and gain a more uniform classification of this subject. He spoke repeatedly at the Academy on neuro-ophthalmology in his instructional courses.

In his private practice, he had seen some 70 cases of angoid streaks and was ever searching for the true etiologic factor in these cases. He was an excellent operator, skillful and technically sound. His contributions to ophthalmic literature showed originality, careful preparation, and a thorough knowledge of his subject. An enthusiastic and a forceful speaker, he was a frequent and popular guest at society and post-graduate meetings where his friendliness and cordiality made many friends.

One of Dr. Clay's major interests was the underprivileged in the clinics at Grady Hospital and at his plantation locality, Walnut Grove; here, he gave unstintedly for hospitalization and education at his own expense. He loved outdoor life and sports, was an excellent golfer and a good fisherman. His hobby and avocation was his pride in the cattle farm where his fine herd of polled-Hereford cattle thrived. At the time of his death, his farm lands were becoming a model for soil conservation and diversification.

In 1915, Dr. Clay married Eleanor Hall Solomon of Macon, Georgia, who predeceased him by several years. He is survived by his two children, Mrs. Lawson Peel Calhoun, of Atlanta, and Grady Clay, Jr., of Louisville, Kentucky, and by three grandchildren. He was a staunch member of the Methodist faith and the patron of his county church at Walnut Grove.

Those of us who worked by his side loved him, knew his worth as a friend, physician, teacher, and humanitarian. His death in the prime of his life is an irreparable loss, leaving a niche that cannot be well filled.

J. Mason Baird.

BOOK REVIEWS

DIE ERKRANKUNGEN DES AUGENHINTERGRUNDES (DISEASES OF THE EYEGROUND). By Prof. Dr. Adalbert Fuchs. Vienna, Austria, Franz Deuticke, 1943. 300 pages, 66 text illustrations, 44 color plates; German language (only a few copies are available at present).

Material for this exquisitely illustrated and concisely written book was collected during the two decades of the author's intensive activities of teaching, research, and consultations at the University of Vienna. He gives a clear description of the essential findings necessary for correct diagnosis of the common, as well as the rare, diseases of the ocular fundus and emphasizes their relation, if such exists, with the other medical specialties.

One of the best points of the book in the reviewer's opinion is the juxta position of clinical and histopathologic find-

ings, without detailed, nonessential histologic descriptions, creating an indelible association in the reader's mind between the clinical phenomena and the underlying pathologic processes. Nineteen of the 44 color plates are histopathologic illustrations, placed in such a way as to make correlation with the clinical condition extremely simple. The material of the entire book is arranged so well that ease of orientation is one of its most pleasant features. A short clinical history contained in the discussion of each colored illustration adds to the liveliness of presentation.

The book was written during the years 1941 and 1942, under great mental, emotional, and physical stress produced by the war, and Professor Fuchs is to be congratulated upon being able to create this masterpiece under such adverse conditions.

The paper of the book and the plates are of excellent, undoubtedly prewar, quality.

Our sincere congratulations go to Professor Fuchs with the best wishes for his future and that of his beautiful book.

Bertha A. Klien.

PHYSIOLOGIE OCULAIRE CLINIQUE. By A. Magitot. Paris, France, Masson & Cie, 1946. Stiff paper covers, 457 pages, 235 illustrations. Price not stated.

Evidently expecting the book to speak for itself, Magitot has dispensed with preliminary preface and introduction. The volume, well printed, well organized, and very readable, is apparently designed for the beginner in ophthalmology. An author index is lacking, and the bibliography is scanty, inaccurate, and not closely related to the material developed. The seasoned student will miss the assimilation of the latest research, the careful documentation, the encyclopedic detail, and the interpretive insight that so brilliantly characterize Duke-Elder's textbook. Although Magitot, in his earlier chapters, favors unduly many tenuous theories of a previous decade, his treatment of photochemistry is refreshingly different and, surprisingly, includes the latest researches of von Studnitz from Pflüger's Archiv of 1943, in which the iodopsin of Wald is shown actually to consist of three carotenoid complexes homologous to the tripartite system of cone-oil globules found in many birds and reptiles.

In every section, Magitot features an excellent discussion of comparative physiology, and fortunately his stimulating presentation is not relegated to fine print. The author's own numerous researches receive only brief mention but contribute much by giving the volume a personal and authentic flavor.

This book was written under difficult circumstances. The author was in hiding in the south of France, under an assumed name, ignorant of the health and welfare of his family and the state of his property. The liberation of France permitted him to return to Paris where he was united with his family but where, too, he found that the Nazis had ravished his house and library. It is, therefore, all the more remarkable that this excellent work could appear at all.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

1

GENERAL METHODS OF DIAGNOSIS

Hughes, W. L. and Cole, J. G. **Technical uses of air in ophthalmology.** Arch. of Ophth., 1946, v. 35, May, pp. 525-540.

This very practical and excellently arranged article should be read in full. The injection of air into Tenon's capsule helps in localizing intraocular foreign bodies inside or outside the eyeball.

In surgical procedures air has been found of value in several ways. In cases of recent laceration of the cornea with incarceration of iris or lens capsule in the wound, mattress corneal sutures are so placed that an air-tight closure of the wound is obtained.

Anterior synechias are apt to recur after the simple incision of the band. Air forms the ideal substance for prevention. A special knife has been constructed, similar to the goniotomy knife, but with a longer blade, with which it is possible to aspirate the aqueous and insert as much air as is required without removing the knife from the anterior chamber.

Frequently, air can be used after discission of a secondary membrane or after iridotomy. In two patients, after intracapsular cataract extraction, a mound of vitreous protruded through the pupil. The vitreous was separated from the cornea with a suitable curved iris repositor inserted obliquely at the limbus (vitreodialysis) and air was injected to maintain the separation until the aqueous reformed.

As a final step in cataract extraction, injection of air into the anterior chamber helps to prevent incarceration of tissue in the wound.

In a trephine operation for glaucoma, air injected into the anterior chamber provides a space between the iris-lens diaphragm and the cornea, and some of the air passes out of the trephine opening under the conjunctival flap. Here it provides at least a temporary space by separation of the conjunctival flap from the underlying sclera. In the delayed formation of the anterior chamber after trephination or opera-

tion for cataract, air has been injected into the anterior chamber as an aid in its reformation.

Goniotomy, introduced by Barkan for deep chamber glaucoma, has gained only moderate acceptance because of the difficulty attending the manipulation of the heavy contact glass and the knife at the same time. With the technic that is described it is possible to perform goniotomy in glaucomatous eyes with a shallow anterior chamber, as well as in those with a wide angle.

No contact glass is used. It was demonstrated by animal experimentation that a distinct view of the anterior chamber could be obtained if air was substituted for the aqueous. Work on rabbits and on three human eyes is reported.

Koster, in 1902, used air in the anterior chamber as a therapeutic aid in cases of tuberculous iridocyclitis and keratitis. The authors have had no experience with this use of air.

In the operation for detachment of the retina, many authors have described injection of air into the vitreous with the idea of forcing the retina against the choroid.

The injection of air makes a shallow anterior chamber readily accessible to direct inspection with the slit lamp. Diagnostically the injection of air helps to decide whether a shallow chamber is due to an actual increase of vitreous or lens or to vascular congestion of the choroid. It is interesting to speculate on the diagnostic and therapeutic use of various gases that might be used to deter or combat bacterial growth or otherwise affect abnormal intraocular conditions. R. W. Danielson.

Lopez-Enriquez. **Individual films for the Leica camera.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, Feb., pp. 137-138.

A single film carrier for the Leica camera is described. (2 illustrations.)
Ray K. Daily.

Rocha, Hilton. **Cycloplegine.** Rev. Brasileria de Oft., 1946, 4th yr., June, no. 4, pp. 297-301. (See Section 3, Physiologic optics, refraction and color vision.)

2

THERAPEUTICS AND OPERATIONS

Blok, C. J. **Alkaline eyedrops and their stability.** Ophthalmologica, 1944, v. 108, Oct.-Nov., pp. 217-223.

Alkaline eyedrops are active in lower concentration because of better penetration. The stability of such solutions was investigated from a chemical and pharmacologic standpoint. Pilocarpine in boric acid solution showed practically unlimited stability, while alkaline pilocarpine solutions should not be kept longer than six weeks. Alkaline solutions of atropine, homatropine, and scopolamine are much less stable and can be used for only three weeks. Boric acid is to be avoided in the latter solutions. The author recommends the addition of 0.03 percent Nipasol or one drop of chloroform per 10 c.c. of solution for better conservation. Three sample prescriptions for pilocarpine, atropine, and scopolamine are given. (Literature.) Max Hirschfelder.

Cutler, N. L. **A basket type implant for use after enucleation.** Arch. of Ophth., 1946, v. 35, Feb., pp. 71-83. (See Section 13, Eyeball and orbit.)

Danielson, R. W., and Long, J. C. **A method of evisceration of the eyeball.** Amer. Jour. Ophth., 1946, v. 29, July, pp. 859-861. (4 figures, references.)

Dubois-Poulsen, A. **Penicillin in ophthalmology.** Ann. d'Ocul., 1945, v. 178, Dec., pp. 533-555.

The indications and contraindica-

tions of penicillin are now becoming apparent. The tolerance of different tissues varies widely. In the aqueous and cerebrospinal fluid lymphocytosis and fibrogenesis appear as a manifestation of aseptic inflammatory reaction. The therapeutic dose here varies between 200-1,000 units in 0.2 c.c. normal saline solution. The vitreous tolerates approximately 100 units. External applications and instillation of strong solutions have been followed by corneal desquamation. Allergy, though rare, may be local or general, and when it occurs local treatment must be discontinued. Local ocular instillations should be made every two hours during the day and every three hours during the night. The best average strength is 1,000 units per c.c. In severe corneal ulceration penicillin crystals have been applied directly to the wound. The intramuscular or intravenous use is less effective in ocular lesions than the subconjunctival injection of 5,000 units in 1 c.c. of 2-percent procain solution. In iritis, iridocyclitis, and choroiditis, penicillin is of questionable value. This may be owing to the character of the causative organism, the allergic character of the ocular reaction, or to other causes not yet determined. The conjunctival infections with staphylococcus, pneumococcus, the Morax diplobacillus, and the inclusion body infection of the new born, respond to penicillin. Trachoma is apparently not affected by penicillin as much as by sulphonamides. Corneal infections caused by penicillin-sensitive organisms are best treated by subconjunctival injections. In postoperative infection penicillin should be promptly used subconjunctivally or in the anterior chamber, and by local instillation. The eye should be left unbandaged and open as much as possible. The respective indications of penicillin and the sulphonamides have not yet been established. The report supplements another on this subject published earlier in this Journal (Ann. d'Ocul., 1945, v. 178, March, pp. 81). Numerous illustrative cases are presented.

Chas. A. Bahn.

Effect of antiseptics on regeneration of corneal epithelium. Bull. U.S. Army Med. Dept., 1946, p. 257. (See Section 6, Glaucoma and ocular tension.)

Gibson, A., and Carlisle, J. M. **Industrial first aid in chemical injuries of the eye.** Sight-Saving Review, 1945, v. 15, Winter, pp. 220-228.

Immediately after a chemical injury, the patient's eye should be flushed with water at the plant Medical Department. The contents of the conjunctival sac is then tested for its reaction with indicator paper. A local anaesthetic is applied to the eyeball, the lids and conjunctiva are thoroughly cleansed, the cornea is stained with fluorescein, so that these tissues may be examined for abrasions, foreign bodies, lacerations, and chemical burns. Treatment for burns consists of cold compresses, local anasthetics, liberal quantities of penicillin ointment, eye pads, and atropine when needed. For alkali burns, the irrigation should be continued until the secretion remains neutral in reaction. Adhesions should be looked for twice daily.

I. E. Gaynon.

Grosz, Istvan. **Standardization of eye drops.** Acta Ophth., 1944, v. 22, pt. 2, pp. 147-157.

The literature is reviewed and a plea is made for the use of buffered solutions for eye drops. Formulas are given for acid and alkaline buffer solutions, and for the most desirable combinations of

these for the various drugs used in ophthalmology. Ray K. Daily.

Hughes, W. L. and Cole, J. G. **Technical uses of air in ophthalmology.** Arch. of Ophth., 1946, v. 35, May pp. 525-540. (See Section 1, General methods of diagnosis.)

Jones, C. C. **The use of penicillin in diseases of the eye, ear, nose and throat.** J. Iowa M. Soc., 1946, v. 36, May, pp. 193-194.

The inhibitory action of penicillin affects the staphylococcus aureus, hemolytic streptococcus, pneumococcus, gonococcus, and meningococcus. Penicillin inhibits the metabolism of the intracellular enzymes of these organisms. Normal saline solution, or certain buffers are the vehicles of choice. An aqueous solution is said to lose 10 percent of its potency every twenty-four hours at five degrees centigrade.

Penicillin is compatible with all drugs that are used in the external diseases of the eye except adrenalin. It has been used to good advantage (1,000 units per c.c.) in dacryocystitis. Penicillin ointment of the same concentration, instilled every four hours, gives better results than the solution in acute catarrhal infectious conjunctivitis. According to O'Brien, penicillin ointment, 1,000 units per gram, is more effective than 5-percent sulfathiazole when combined with meibomian massage and staphylococcus toxoid desensitization in chronic blepharitis and conjunctivitis. Ulcers of the cornea that are resistant to usual therapy have responded to subconjunctival injections of one half c.c. of penicillin, 1,000 units per c.c. twice daily. The procedure is painful and requires local anaesthesia.

In iontophoresis, a solution of 500 units per c.c. is used for three minutes with a current strength of two milliamperes. I. E. Gaynon.

Kohout, J. J. and Callahan, Alston. **Ophthalmopedics.** Amer. Jour. Ophth., 1946, v. 29, Aug., pp. 968-976. (13 figures.)

Law, T. B. **Penicillin in preoperative and postoperative ophthalmic surgery.** M. J. Australia, 1946, v. 1, March 30, p. 442.

A violent reaction resembling early panophthalmitis occurred in a patient after a cataract extraction. Intensive penicillin therapy was instituted immediately. The drug was given intramuscularly (100,000 units in 6 hours), and was also instilled into the conjunctival sac every hour. Within eight hours the eye cleared remarkably and there was uneventful recovery.

The second patient, a man aged 75 years, had a mature cataract, a marked chronic conjunctivitis with muco-purulent discharge, and a history of chronic purulent sinusitis. Repeated conjunctival cultures showed as many as 30 colonies of staphylococcus aureus. Penicillin was instilled in the conjunctival sac every hour for 10 hours, when the sac was found to be sterile. The tear sac was removed despite the fact that it was free from discharge. The cataract was removed after five hourly instillations of penicillin solution and there was uneventful recovery. On departure from the hospital two weeks later 30 colonies of staphylococcus aureus were found in cultures.

F. M. Crage.

Moreu, Angel. **The use of pre-anesthetic medication in ophthalmology.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, Feb., pp. 134-137.

The author warns against the use of Escofedal and Penumbrol in vagotonic subjects, in whom the administration of these drugs may produce an alarming drop in blood pressure, and bradycardia. A 500c.c. blood transfusion controlled the symptoms in a patient with an alarming drop of blood pressure and a barely perceptible pulse. The author urges thorough general examination of the cardiovascular system, a preliminary administration of a cardiovascular stimulant, and preparedness to meet cardiovascular complications.

Ray K. Daily.

Pinticart de W., Elcira, **Tuberculin therapy in Chile.** Rev. Brasileira de Oft., 1946, 4th yr., June, no. 4, pp. 303-312.

The author uses a series of tuberculin dilutions, the weakest of which are extremely attenuated, and which he numbers according to the number of zeros contained in the strength of the dilution; for example, the description in numerals of number 20 solution being unity followed by twenty zeroes. (References.) W. H. Crisp.

Schmid, A. E. **The distribution of Irgamid in the tissues and fluids of the** eyeball. Ophthalmologica, 1943, v. 106, Nov.-Dec., pp. 289-300.

Irgamid is a sulfanilamide derivative that the author used in experiments on young rabbits.

The Irgamid was used locally in the form of a powder or of a 15-percent ointment, was introduced through a stomach-tube or was injected in a 20-percent aqueous solution into the marginal vein of the ear.

The eyeballs were examined immediately after the death of the animal and the drug content of the individual ocular structures was determined by the method of Pulver. The concentrations varied considerably with the method and time of administration. The variations from individual to individual were unessential.

Local administration gives a remarkable concentration in the anterior chamber and in the strongly vascularized tissues of the eyeball. This concentration is greater, when the corneal epithelium is damaged, in all tissues except the lens. In the lens the drug concentration, which is usually small, is even smaller in corneal erosions. The concentrations after administration in the powdered form rise rapidly and are rather high. They are lower and of longer duration after using the ointment. Administration four times per day results in the greatest concentration.

In peroral administration the maximum concentration was attained after 10 hours. The conjunctiva, the vitreous, and especially the choroid and retina manifested high concentration and slow elimination.

Intravenous application produced a rapid concentration of the drug in all ocular tissues and fluids, particularly in the vitreous. (9 tables and curves, references.) Alice R. Deutsch.

Schultz, A. **Ocular dermatitis from local penicillin.** Arch. of Ophth., 1946, v. 35, Feb., pp. 145-149.

Of 52 cases of eye disease treated by the local application of penicillin, two developed symptoms of local tissue hypersensitivity. The eyes were treated with sodium penicillin in salt solution or in ointment in concentrations ranging from 500 to 3,000 units per gm. In the two cases reported ocular dermatitis developed. In the first instance the condition resembled acute dermatitis due to atropine, while in the second

case it simulated contact dermatitis. The allergic reactions gradually subsided with cessation of treatment with the drug. John C. Long.

Struble, G. C. and Bellows, J. G. **Contact eye cup for corneal baths with solutions of penicillin.** Arch. of Ophth., 1946, v. 35, Feb., pp. 173-175.

Simple instillation of penicillin eye drops will effect a prompt cure of the acute inflammatory diseases of the conjunctiva caused by penicillin-sensitive organisms. Simple instillation is not adequate in corneal ulcers, particularly if the deep layers of the cornea are involved. A special contact eye cup is described which is made of clear acrylic material. It can be fitted over the eyeball and a small flat handle projects between the lids. The cup has two holes, one for filling it and the other for the escape of air. With the patient in a sitting or reclining position and the eye anesthetized, the cup is inserted and filled with penicillin solution by means of a syringe. The cup is then left in place for one-half to one hour. There is no loss of solution through the lacrimal apparatus nor is there dilution by the tears. The transparent cup permits view of the anterior segment of the globe and the level of the penicillin solution at all times. The contact cup fits both eyes. Illustrated.

John C. Long.

Vejdovský, V. **Some experiences with penicillin in eye diseases.** Lékařské Listy, 1946, v. 1, April 1, pp. 101-104.

This is the first report on penicillin therapy in ophthalmology from central Europe. In two infants with gonorrhoeal ophthalmia of the newborn 30,000 units were used and in three adults with gonorrhoeal eye affections 100,000 units were followed by recovery. An infected eye with a perforating wound, and an eye with postoperative iridocyclitis recovered after subconjunctival and intramuscular applications of penicillin. Penicillin was also effective in an eye with a serpigenous corneal ulcer. O. Felsenfeld.

3

PHYSIOLOGIC OPTICS, REFRACTION, AND COLOR VISION

Angius, T. **Experimental studies of night blindness.** Rassegna Ital. d'Ottal., 1946, v. 15, no. 1 and 2, p. 11.

A group of 51 healthy men between 18 and 21 years of age were studied daily for several weeks to determine the effects of vitamin A upon their light threshold. It was concluded that vitamin A has a specific action, especially to increase the perception of form. The action is either catalytic, favoring the power of fatigued tissue to recuperate, or an augmentation of vitamins to rebuild the visual purple. Vitamin A is therefore indicated in those individuals who need to lower their light threshold and in those who are unduly fatigued or exposed to intense light. (6 figures, 1 table.) Eugene M. Blake.

Bateman, Eric. **The Cantonnet system from the viewpoint of general psychology.** The Optician, 1946, v. III, Feb. 15, pp. 46-47.

The unilateral repression of an image can be likened to the repression that occurs in the mind when faced with a situation which it finds intolerable. The eye deviates to displace an offending image and the mind at a higher level represses the image, and represses it still more at the macula to keep the eye from turning back. A discussion is given of the ego, the subconscious level, and the conscious level. Apply-

ing the principles of psychology, the treatment consists of a careful refraction, correction of the amblyopia as much as possible, exercises to overcome repression or, as Cantonnet calls it, neutralization, and the development of simultaneous and stereoscopic vision. I. E. Gaynon.

Clark, Brant, Johnson, M. L., and Dreher, R. E. **The effect of sunlight on dark adaptation.** Amer. Jour. Ophth., 1946, v. 29, July, pp. 828-836. (5 figures, 3 tables, references.)

Crawford, B. H. **Photochemical laws and visual phenomena.** Proceedings Royal Society Series B, 1946, v. 133, Jan. 10, pp. 63-75.

Foveal and parafoveal light reactions and recovery of dark adaptation were studied. The explanation of visual phenomena remains undetermined as long as the theory of the kinetics of chemical reactions, upon which they depend, remains unsettled.

F. M. Crage.

Dudragne, R. A. **Physiologic amplitude of accommodation and false accommodation of the aphakic eye.** Ann. d'Ocul., 1945, v. 178, Sept.-Oct., pp. 377-398, 441-452.

The subject is discussed under the following headings: correction of anetropia; corrected accommodation in ametropia; complete correction of the eye; depth of the field of the eye; spheric aberration of the eye; punctum remotum and pupillary opening; physiologic accommodation of the aphakic eye; experimental studies.

The mathematical analysis of each topic is presented in detail. Increased size of the pupil in twilight may increase the focal power of the eye as much as two diopters. Some of the factors involved in accommodation are best studied in the aphakic eye in which a false accommodation may be as great as five diopters. Among the factors that bring it about are: the distance of correcting lenses from the cornea; astigmatism that is caused by angulation of correcting lenses; unequal focal power of different sectors of the cornea; occupational familiarity with the interpretation of images; pressure on the eye by the lids; depth of the visual field; and spheric aberration of the eye. Chas. A. Bahn.

Gonzales, J. B. **Dark adaptation in pregnancy.** Arch. de la Soc. Oft. Hisp.-Amer., 1945, v. 5, Feb., pp. 120-128.

Forty women in the second half of pregnancy were examined with the Birch-Hirschfeld adaptometer. Their adaptation curves, while within physiologic limits, are somewhat inferior to the normal controls. Eight percent of the patients had definitely subnormal adaptation curves, but none of them had subjective hemeralopia. The adaptation of women on diets adequate in vitamin A were no different from those on inadequate diets. The adaptation curves show no variation during the months of the second half of pregnancy. (Adaptation curves.)

Ray K. Daily.

Göthlin, G. F. **Inhibitory processes in the normal mechanism of the color sense.** Ophthalmologica, 1944, v. 107, March-Apr., pp. 158-177.

From his experiments the author concludes that the fundamental color sensations of man are red, green, and blue, not violet. From observations when mixing complementary colors in different proportions, and from the existence of negative ordinates in Maxwell's and Wright's graphically ex-

pressed measurements of three-color synthesis of spectral monochromatic colors, the author infers that each excitatory impulse that proceeds from the color receptors is accompanied by an inhibitory nerve impulse to the substratum of its complementary color. It is assumed that the sensation of yellow results from a central coordination of impulses which come from the red and green receptors. This synthetic yellow plus fundamental blue, if the impulses are equally strong, give the sensation of white. The author expresses the opinion that the negative afterimage has its origin in elements that were inhibited during the presentation of the positive color and spontaneously come into a state of excitation after the positive color disappears. The differences between the author's hypothesis and the theories of Young-Helmholtz and of Hering are discussed. (Bibliography.) Max Hirschfelder.

Göthlin, G. F. **An analysis of the perception defect in published and spectroscopically investigated cases of congenital tritanopia.** Acta Ophth., 1943, v. 21, pt. 1-2, pp. 88-96.

An analysis of the published cases of congenital yellow-blue blindness shows that they form two different categories. One group of blue-blind subjects have color sensations from the violet part of the spectrum. The second group is both violet and blue blind, and also has a simultaneous weakening of perception of long-wave red. This later group therefore comprises the pure cases of tritanopia. One of the two typical tritanopic subjects examined saw spectral violet as pale red, and the other as red dotted with small black spots. These data indicate that violet is a product of simultaneous stimulation of blue and red. The fact that in the absence of blue perception violet takes on the character of red gives further support to the author's contention that violet is a product of simultaneous fundamental sensations of blue and red.

Ray K. Daily.

Göthlin, G. F. **Participation of central inhibitory processes in the synthesis of color sensations. A working hypothesis.** Acta Ophth., 1943, v. 21, pts. 1-2, pp. 75-87.

With the help of a double-balance model, Göthlin outlines his theory of color perception, which assumes that every impulse from retinal receptors for a color sensation is always combined with a certain degree of central inhibition of the complementary color in the same area. According to his theory the sensation of white is developed in two stages; in the first a balance between impulses for red and green produces yellow; in the second yellow and blue produce white. This theory, contrary to the Young-Helmholtz theory considers blue as a fundamental color, and differs from Hering's theory in assuming that yellow is the result of central synthesis of green and red, and denying that red and green are complementary colors. For experimental evidence supporting his theory reference is made to the Journ. of Phys. v. 57, and to the Handlingar of the Swedish Academy of Science, Ser. 14, v. 20: 7. Ray K. Daily.

Hardy, L. H., Rand, G. and Rittler, M. C. **Tests for detection and analysis of color blindness.** Arch. of Ophth., 1946, v, 35, Feb., pp. 109-119.

This is a report of data collected in the study of 106 persons with defective color vision of varying types and amounts by means of various editions of the Ishihara test for color blindness.

A comparison of the average scores and the range of scores for the different types of deficiency in color vision does not show notable differences in the fifth, seventh and ninth (British reprint) editions of the Ishihara test. Properly administered, the three editions of the test afford a good rough device for screening persons with defective from persons with normal color vision if a performance score of 60 is taken as the critical score. A critical score cannot be established for the 10 Ishihara plates reproduced in the American Optical Company's test. Tested with this group of plates, some subjects with defective color vision passed all the plates and some with low normal color vision passed only six of the plates. John C. Long.

Hartridge, H. **Recent advances in the physiology of vision.** Brit. M. J., 1946, April 27th, pp. 637-638.

Goldman and Hagan measured the length of the eyeball by passing a beam of X rays through a slit in a stout metal plate. A narrow ray is produced that falls on the observer's dark adapted eye at right angles to its optic axis. A beam of light is seen concentric with the fovea. As the beam moves backward in the eye, it becomes narrowed to a point and coincides with the most posterior part of the retina. The beam is then moved forward until it coincides with the anterior part of the cornea. The movement is carefully measured. Total refraction of the eye is measured by the following procedure. Two narrow beams, five millimeters apart, are projected in at the front of the eye just below the line of sight. Two narrow beams are projected by an optical lantern on a screen and are adjusted until they coincide with the X-ray images. The distances are carefully measured. Total refraction in diopters equals 1000 times distance between lantern beams divided by screen distance times the distance between X rays. Their mean values are as follows: length of eyeball equals 24.05 millimeters; total refraction equals 58.75 diopters; nodal distance equals 17.02 millimeters; posterior focal distance equals 22.73 millimeters.

Granit's work on the micro-electrode experiments depends upon the principle that when a sensory nerve is stimulated, it undergoes a change of electrical potential. The retina of an animal is exposed and a single optic nerve fiber is stimulated and the change in potential measured. He found eight types of receptors. Type 1 is the dominator; the remaining seven are called modulators. There is one modulator for orange, one for yellow, three types for different shades of green, and two for blue.

Using the Landolt ring test, Schlaer found little difference in the visual acuity when lights of different colors were compared to white. An experiment is also described wherein the spurious colors of chromatic aberration are eliminated by a nervous process called the antichromatic response.

I. E. Gaynon.

Hylkema, B. S. **Examination of the visual field by determining the fusion frequency.** Acta Ophth., 1942, v. 20, pt. 2, pp. 181-193.

This investigation was made by arranging the test-field in the form of a campimeter, and taking the fusion frequency at various areas in the field. The graphically recorded data show that there is a region of low fusion frequency in the vicinity of the blind spot. The fusion frequency is lower in the upper than in the lower part of the field. The highest figure is found nasal-

ly and the lowest temporally. In normal binocular vision the temporal downward area in the visual field of one eye corresponds to the nasal downward area of the contralateral eye. Therefore, when an object is less than 30 degrees from the fixation point, the function of the eye, which fixates the object nasally, must predominate. If the object lies to the right, the left eye predominates. When the object is farther in the periphery, the eye on the same side takes over the task. The fusion frequency test demonstrates more effectively than any other test the predominance of one half of the visual field over the other. Ray K. Daily.

Hylkema, B. S. **Fusion frequency with intermittent light under various circumstances.** Acta Ophth., 1942, v. 20, pt. 2, pp. 159-180.

This investigation on the fusion frequency discusses the frequency at high light intensities, and with interaction. It was found that the fusion frequency peak is formed under an illumination of 200 to 800 candle power per square meter. The author suggests that this light intensity might represent the optimum illumination for visual functioning, and serve in the evaluation of lighting conditions. After reaching this peak, further increase in light intensity results in a drop in the fusion frequency; at the state of adaptation at which the fusion frequency curve drops signs of dazzling appear. The diminished color sensitivity associated with dazzling and the lowered fusion frequency point to a temporarily impaired visual function.

Interaction was investigated with the use of two or four intermittently illuminated test fields, syncronously or in opposing phases. The charted results show that interaction is stronger in the periphery than in the center; it is effective across a longer distance in the periphery, up to five degrees, which corresponds to 0.5 millimeters on the retina. The experiments show that in addition to the light intensity, the size of the illuminated area is also a factor in the fusion frequency. An attempt was made to ascertain the degree of cerebral influence on the fusion frequency by making observations monocularly and binocularly. The figures obtained with one or both eyes differ but little from each other. This is interpreted to indicate that by far the larger share in this process is taken by the retina, and that the cortical influence is slight. Light intensity produces its effect largely in the retina. Area effect and interaction is ascribed to the associative nervous system of the retina. The state of adaptation is determined by the outer layer of the retina, and perhaps also by the central nervous system. Local adaptation that occurs with a long exposure is largely a cerebral process. Ray K. Daily.

Khan, N. E. **Vitamin A and night vision.** Indian Med. Gazette, 1945, v. 80, Dec., p. 608.

Dark adaptation studies were made in 190 British Military Personnel and 1,090 Indian soldiers. Sankaran's photometer showed defective dark adaptation in 14 percent of the British and 29.2 percent of the Indian soldiers. Thirty-eight (3.5 percent) of the latter complained of night blindness although there were only two who could not see in the dark. This condition therefore is not as common as is supposed. All but one of the 26 Indians treated with vitamized oil developed normal dark adaptation within two weeks.

Recent data on Vitamin A are discussed. Greater use of carrots and

greens of the spinach type, such as saks, is suggested to improve Indian nutrition. F. M. Crage.

Mann, Ida, and Sharpley, F. W. **The normal visual (rod) field of the dark adapted eye.** Jour. Physiol., 1946, v. 104, April 15, pp. 384-391.

The authors tested one eye of each of 47 subjects after dark adaptation. They used a perimeter of 33-cm. radius, a radium target below the cone threshold as stimulus, and a red light for fixation point. The angular radius, that is the angular distance from the center of the plotted field, was calculated as an average of the plotted values of the 24 meridians at 15-degree intervals. The size of field seemed to decrease with increase in age of subject. The fields differed considerably in shape, but the area as expressed in terms of its mean angular radius was fairly constant. Low errors of refraction apparently were negligible. (2 tables, 2 figures, references.)

Bennett W. Muir.

Martin, D. H. H. **Some refinements in cross cylinder technique.** The Optician, v. 111, May 24, 1946, p. 330.

The writer uses the cross cylinder because it puts less demand on the intelligence of the patient, is more rapid, and blends well with the objective examination.

Certain test letters are recommended for the testing of the axis. For estimating axis direction at approximately 90 or 180 degrees, he recommends the letters E, F, H, L, and T; to estimate axis direction at 45 or 135 degrees the letters V, W, X, and Y, and to test cylinder power in the same positions the letters E, F, H, L, and T.

I. E. Gaynon.

Matteucci, P. **Quantitative and qualitative perimetric studies with monochromatic and white targets.** Rassegna Ital., d'Ottal., 1946, v. 15, no. 1 and 2, p. 26.

Using monochromatic and white targets of equal subjective brilliance revealed findings quite diverse from those of previous investigators. The threshold of light was determined in each subject by photometric measurements. With equality of size, saturation, and brilliance of the target used, and with minimal variations of illumination and of adaptation, important modifications of the peripheral limits for colors were found.

Varying degrees of sensibility of the retina for a single color and other factors not easily controllable make it difficult to define exactly the peripheral limits for colors. The author expresses doubt as to the utility of clinical perimetry with colors. (1 figure.)

Eugene M. Blade.

Parker, F. W. **Studies on dark adaptation in military personnel complaining of "night blindness."** Arch. of Ophth., 1946, v. 35, May, pp. 555-571.

A fairly common complaint of patients seen by the ophthalmologic service at the front is poor night vision.

Sixty-six patients were examined with a Nagel adaptometer for determination of dark adaptation. Careful ophthalmologic examinations were made, and neuropsychiatric consultation was secured when indicated. Thirty-nine patients of the group complained of moderate to extreme night blindness. Fourteen had no ocular complaints, and 13 were patients with hepatitis. Of the 14 patients with no ocular complaints, all showed normal adaptation curves. Of the 39 patients

who complained of night blindness, 5 with moderate complaints showed normal dark adaptation, and three of these had more than 1.50 D. of astigmatism. For six others with normal readings but severe complaints detailed histories revealed some incident that had caused the patient to believe that his night vision was inadequate. The remaining 28 of the 39 patients had initial low readings for dark adaptation. No cause for this could be found in 5 patients, and these men were considered to have true simple hemeralopia; 4 had a pathologic condition of the fundus; 5 patients proved to be malingering, and 14 were psychoneurotic. Of the 19 patients who were malingerers or psychoneurotic, 11 had corrected vision of 20/40 or less, and 12 had refractive errors of above 1.50 D.

A test for malingering is described which utilizes opticokinetic nystagmus.

Six patients with chronic disease of the liver showed subnormal dark adaptation. Three of these persons were given oral vitamin A therapy, with pronounced improvement. Six patients with infectious hepatitis, whose disease did not become chronic and whose hospitalization did not exceed 15 weeks, showed normal dark adaptation curves.

R. W. Danielson.

Pescatore, C. **The operation of Fukala in high myopia.** Rassegna Ital. d'Ottal., 1946, v. 15, no. 1 and 2, p. 48.

The author reports six cases of high myopia in which clear lenses were removed by aspiration. He concludes that the operation is not free from severe postoperative complications, but that the improvement in vision warrants the risks. The best time for operation is between 8 and 20 years of age, and the operation is most successful in eyes with about 20 diopters of myopia. Fundus changes are not a contraindication to the operation and discission of the capsule is usually required.

Eugene M. Blake.

Pincus, M. H. **Unaided visual acuities correlated with refractive errors.** Amer. Jour. Ophth., 1946, v. 29, July, pp. 853-858. (2 tables, reference.)

Rand, G. **Relation between illumination and visual efficiency.** Arch. of Ophth., 1946, v. 35, May, pp. 509-513.

Rand quotes Weston's investigation which was undertaken to test the value of a method suggested by Beutell for determining the level of illumination required for the efficient performance of work that involves visual discrimination. The method is based on the proposition that the illumination required for any visual task, as compared with the simplest possible task, depends on certain conditions adversely affecting its performance, that these conditions can be defined, and that if the relationship can be ascertained between each of the conditions and the illumination required to compensate for it, then the illumination suitable for the performance of the task ought to be capable of actual computation.

A discussion of the various factors involved in illumination and visual efficiency is given.

From a practical point of view, Weston's studies and those of Ferree and Rand show that level of illumination cannot compensate entirely for the adverse conditions of small size of detail and poor contrast in the work. When the task is such that these factors cannot be improved the level of illumination should be made as high as is compatible with other factors of good

lighting, such as freedom from high brightness and high brightness ratios in the field of view. In most cases of this type it is likely that the most favorable illumination will be furnished by a good general level of background illumination, free from glare and high brightness ratios, supplemented by local lighting of the immediate task, the source of which must be well shielded from the eyes of the worker.

R. W. Danielson.

Redlich, F. C., Callahan, A. and Mendelson, R. H. **Electroencephalographic change after eye opening and visual stimulation.** Yale J. Biol. and Med., 1946, v. 18, May, pp. 367-376.

In a study of 100 subjects, the electroencephalographic changes upon eye opening, which were not uniform, were characterized mainly by a decrease of amplitude and less by increase in frequency of the occipital rhythm. These changes were usually reversed by closing the eye. Three patients with bilateral blindness showed no changes. The effect on the electroencephalogram caused by the opening and closing of the eye does not permit a consistently valid differentiation between true and hysterical, and malingered blindness. (1 table, 4 figures, references.)

Bennett W. Muir.

Rocha, Hilton. **Cycloplegine (Benzoil-diethyl-aminol-ethanol).** Rev. Brasileira de Oft., 1946, 4th yr., June, no. 4, pp. 297-301.

This substance is one of those recently proposed as substitutes for homatropine, to which they are considered superior in regard to brevity of action and of speedy return to normal. Parenthetically, credit is given to Swan and White for their studies of di-n-butylcarbaminoilcholine. The author concludes that cycloplegine is "on the right track," and that in certain special aspects it is very superior to homatropine and atropine, although he admits that it shows a striking tendency to cause lacrimation, which may interfere with the usefulness of the drug.

W. H. Crisp.

Sorensen, S. K. **Lenticular astigmatism, designated as the difference between total and corneal astigmatism, illustrated by an examination of its variations with age.** Acta Ophth., 1944, v. 22, pt. 4, pp. 341-385.

In this laboratory investigation the corneal astigmatism was measured with the ophthalmometer and total astigmatism with the refractometer. The graphically presented data and the calculations based on them lead to the following conclusions. Corneal astigmatism is the most important factor in total astigmatism. In corneal astigmatism against the rule the total astigmatism is against the rule and greater than the corneal astigmatism. In the absence of corneal astigmatism a small degree of total astigmatism against the rule is generally present. With weak corneal astigmatism with the rule one usually finds a total weak astigmatism against the rule or no astigmatism at all. In moderately high corneal astigmatism with the rule, the total astigmatism is also with the rule but lower than the corneal. In very high corneal astigmatism with the rule one often finds a high total astigmatism. The total astigmatism shifts with age so as to bring an increased astigmatism against the rule. The corenal astigmatism varies within wide limits. In children and young people 0.75 D. of astigmatism with the rule may be considered physiologic and 0.50-0.75 D. is physiologic in older persons. At 50 to

60 years of age no astigmatism or very weak corneal astigmatism with or against the rule is physiologic. In the aged weak astigmatism against the rule is most frequent. Thus it is seen that the senile corneal changes direct the corneal astigmatism against the rule. Lenticular astigmatism is very frequent; usually it is very weak, but it may reach considerable proportions. The strongest lenticular astigmatism found was 2.00 D. Lenticular astigmatism is usually against the rule. In children and young people 0.75 D. of lenticular astigmatism against the rule is physiologic. In older people 0.50 D. lenticular astigmatism against the rule is common. In the aged lenticular astigmatism usually does not exceed 0.25-0.50 D. against the rule. Weak degrees of corneal astigmatism with the rule are usually compensated by lenticular astigmatism against the rule. Moderately high corneal astigmatism with the rule is partially neutralized by lenticular astigmatism against the rule. In high corneal astigmatism the lenticular astigmatism is usually of the same type. Corneal astigmatism against the rule is usually associated with lenticular astigmatism against the rule. With age the lenticular changes modify the refraction of the lens in the direction of astigmatism with the rule. Lenticular astigmatism is very variable and in determining refraction the total astigmatism should be considered. (13 graphs.) Ray K. Daily.

Stenstrom, Solve. **A new method for exposing unilateral simulated reduction in visual acuity.** Acta Ophth., 1943, v. 21, pt. 3, pp. 237-244.

The method utilizes crossed polarization spectacles and a polarized filter in front of an illuminated transparent chart. The manipulation of the filter from behind the housing which contains the chart, lamp, and filter enables the examiner to transfer the visibility of the chart from one eye to the other without the patient's knowledge.

Ray K. Daily.

Still, D. C. **The calculation of lens effectivity and astigmatic difference at near.** The Optician, 1946, v. 111, Feb. 15, pp. 43-45.

This article does not lend itself to abstracting. The mathematics of lens effectively for far and near is carried out for plus and minus spheres and cylinders to explain the difference in power of astigmatic corrections for distance and for near work.

I. E. Gaynon.

Swaine, W. **The arithmetic of thin lenses. Conjugate foci.** The Optician, 1946, v. 111, May 24, pp. 327-329.

The excess of vergency of the refracted rays above the incident rays is constant and equal to the power of the lens. Using the formula L plus F equals L; where L equals image distance, F equals the focal length of the lens and L equals the object distance, the author demonstrates how the formula may be easily remembered as the path of rays passes from the object through the lens to the image. I. E. Gaynon.

Ten Doesschate, J. **The relation between visual acuity and the differential threshold of brightness sensation.** Ophthalmologica, 1944, v. 108, Oct.-Nov., pp. 187-209.

The differential threshold in comparing two brightnesses B and B′ is determined under such conditions that the brightness B fills the whole visual field (inside wall of a globe) while B′ is being observed in the shape of a circular testfield (visual angle g) with foveal fixation. B′ is projected through an

opening in the globe on B. It is found that the differential sensitivity increases with an increase in B and with an increase of the visual angle. The stage of adaptation influences the differential sensitivity, as the differential sensitivity is diminished in an eye which is not adapted to a lesser general brightness B. It is shown that visual acuity and differential sensitivity depend in an identical way on the brightness B. The results of the experiments are in accordance with recent calculations of de Vries, which take into account the statistical fluctuations in the number of light quanta, which are projected on the different retinal regions. (Bibliography.) Max Hirschfelder.

Wartenberg, R. **Associated movements in the oculomotor and facial muscles.** Arch. Neurol. and Psychiat., 1946, v. 55, May, pp. 439-488.

Based upon the study of four patients, a critical analysis is presented of the commonly accepted hypothesis that associated movements in the territory of the third nerve are due to a misdirection of regenerating fibers. It is suggested that the release phenomenon of Hughlings Jackson more accurately explains these phenomena. After incomplete recovery from third nerve paralysis abnormal phenomena occur, such as the retraction of the upper lid with downward rotation of the globe (pseudo-Graefe phenomenon), and pathologic vasomotor and secretory phenomena. The author gives many reasons why the misdirection theory is untenable. The phenomenon occurs when there has been no trauma to the nerve, or before regeneration could have occurred, or as a congenital anomaly. Once established it is present for life. Associated movements are compared with the symptoms of pyramidal tract lesions, and are found to be similar. The author says "The hypothesis of released phenomenon propounded here, though it may appear somewhat hazardous, seems to be a workable, expandable one, capable of providing further supporting argumentation." (Photographs, references.) Bennett W. Muir.

4

OCULAR MOVEMENTS

Bender, M. B. and Teuber, H. L. **Nystagmoid movements and visual perception, their interrelation in monocular diplopia.** Arch. Neuro. and Psychiat., 1946, v. 55, May, pp. 511-529.

Two cases of transient monocular diplopia were studied. It is concluded that the nystagmoid ocular movements which are associated with fixation are necessary but are not sufficient for the development of monocular diplopia. (3 figures, references.) Bennett W. Muir.

Bertotto, E. V. **Congenital paralysis of the lateral rectus and melanosis bulbi.** Anales Argentinos de Oft., 1945, v. 6, Apr.-May-June, pp. 60-62.

The left eye of an 18-year-old youth had a visual acuity of 6/6, the skin of the lids and the sclera were discolored a slaty gray, the iris was heterochromic, and the lateral rectus was paralyzed, though no diplopia was present. The fundus was normal. The author offers no treatment, and gives a good prognosis. Edward Saskin.

Broendstrup, Poul. **The squinting position of weak-sighted eyes.** Acta Ophth., 1944, v. 22, pt. 4, pp. 386-393.

The material of this investigation comprises 162 patients with impairment of vision in one eye, and normal

visual acuity in the other. The cause of the impaired vision was spontaneous or traumatic unilateral cataract. Most eyes had been operated upon and were aphakic. The material was divided into 3 groups: congenital cataracts, cataracts acquired before the tenth year of life, and those acquired after the age of 11 years. The data of group one indicate that convergence is the position of rest in early childhood, and divergence dominates the picture later. The data of the second group indicate that the older the individual is at the onset of the cataract, and the longer the amblyopic period, the more will divergence dominate as a position of rest. In patients affected under five years of age divergence and convergence will be equally frequent during the first 12 years. If defective vision sets in after the age of five years divergence will be the dominant position of rest. In group three divergence is the dominant position. The data show that when binocular vision is abolished because of unilateral visual impairment the axes of the eyes rarely remain parallel, and that the deviation continues to change for many years. (3 graphs.)

Ray K. Daily.

Foster, J., and Pemberton, E. C. **Effect of operative alterations in the height of the external rectus insertion.** Brit. Jour. Ophth., 1946, v. 30, Feb., pp. 88-92.

In 26 patients who were to have surgery for strabismus, careful measurement revealed vertical phorias of varying amounts. At operation the external rectus, in addition to being advanced or recessed, was raised or lowered on the sclera. Elevation of the muscle raised the eye and lowering it depressed the eye. The results apparently justify the procedure. The measurements of the muscle functions in each patient are presented in tabular form.

Morris Kaplan.

Gallo, L. A., and Novick, R. **Paralysis of the external rectus. Its treatment with transplants from the superior and inferior recti.** Anales Argentinos de Oft., 1945, v. 6, July-Aug.-Sept., pp. 101-103.

Paralysis of the right lateral rectus muscle appeared in a girl, 19 years of age, after typhoid fever. To overcome it a 6-mm. recession of the internus was done, a temporal slip from the inferior rectus muscle and the superior rectus was attached to the insertion of the lateral rectus, and the latter muscle was advanced. Sixty degrees of abduction was achieved. (1 illustration.)

Edward Saskin.

Gibson, H. W. **The spheres of orthoptics and survery in the treatment of strabismus.** The Optician, 1946, v. 111, June 21, pp. 413-415.

The primary aim of all treatment of strabismus should be the restoration of normal binocular stereoscopic vision. Orthoptic treatment alone is indicated when the ocular muscles are not affected by malformation, paralysis, or paresis. Surgery alone seldom restores binocular stereoscopic vision. It is cosmetic in effect and is used alone when conditions are unfavorable for the attainment of stereopsis. In preoperative orthoptic treatment one strives to eliminate suppression and to teach the patient to learn to use both eyes simultaneously. Post-operative orthoptic treatment ensures accurate alignment of the visual axis with the establishment of stereopsis. I. E. Gaynon.

Nordlow, V. W. **The pathogenesis and early operation of constant con-**

vergent strabismus. Acta Ophth., 1945, v. 23, pt. 2, pp. 97-125.

Nordlow favors early operation, and this study contains the tabulated observations on 23 children who were operated upon early. They were in their second year or older when the strabismus was noticed. At operation the youngest patient was not quite two years old, and the oldest just over eight. The operation consisted of a bilateral partial tenotomy of the internal rectus muscles and resection of the external rectus. The author concludes that early operation cures the strabismus and leads to binocular vision in 91 percent of patients. The strabismus is believed to be a hereditary defect. (7 illustrations.) Ray K. Daily.

Nordlow, Waldemar. **The pathogenesis of convergent strabismus.** Acta Ophth., 1942, supplement 20, pp. 134.

The objective of this monograph is to assess the role of refraction, fusion, and mechanical factors in the pathogenesis of internal strabismus. The data obtained by an examination of 105 normal children, seven to nine years of age, 100 normal adults between 23 and 40, and 334 patients with strabismus under 40 years of age are analyzed. The examinations determined the angle of squint, the position of the visual lines, the range of motility, refraction, retinal correspondence, and range of accommodation. The history furnished data on the age at the onset of squint, the course of the strabismus, and the concurrent occurrence of disease. The findings show that normally there is no significant difference in the range of horizonal motility in children and adults. In squinters the primary angle of strabismus at 5 meters was most constant and chosen for comparative study. After the elimination of doubtful cases, paresis appeared to be a factor in 17.5 percent. In 59.4 percent the angle of strabismus was dependent on the accommodation.

In 177 older patients with strabismus the range of ocular motility was normal in extent in both eyes, but shifted inwards. In 66 percent of these the shift corresponded with the primary angle of strabismus. In as much as the shift can be accounted for only by a mechanical abnormality, it is probable that the mechanical abnormality is also the cause of the strabismus. In 30.5 percent the shift of ocular motility was less in extent than the angle of strabismus and in 3.4 percent it was greater. In 138 patients with permanent strabismus over eight years of age 15.9 percent had normal retinal correspondence. The age at the onset of strabismus differed from that found by Smith and Worth. The frequency in this material was highest in the first year, and gradually diminished to the eighth year. In strabismus noted at birth the factors accounting for it must have been present at birth or earlier. Of 253 patients under seven years of age, 97.8 percent were hyperopic, 1.4 percent emmetropic, and 0.8 percent myopic. In 42 patients seen in their first year of life atropinization and the wearing of the refractive correction had no effect on the angle of strabismus, which indicates the action of a mechanical factor in the genesis of the squint. In 58 percent of the patients the ability to fuse appears to have existed at the onset of squint. All patients with periodic squint had a fusion faculty. Illness preceded the onset of squint in 11.8 percent of the patients; in these there is the possibility of a disturbance of fusion due to meningitis or encephalitis. The author concludes that a mechanical factor which can produce a

deviation of the visual axis even in the presence of the fusion faculty is present at the onset of permanent strabismus. In half of the cases a disturbance of fusion did not appear to be a factor. Periodic strabismus can be differentiated into two types. In one type the deviation can be attributed solely to a mechanical factor and in the other type a refractive error also plays a part. (31 tables.) Ray K. Daily.

Nordlow, W. A. **An instrument for measuring the muscle resection in strabismus operations.** Acta Ophth., 1944, v. 22, pt. 1, pp. 49-51.

The instrument consists of a strabismus hook calibrated in millimeters and a muscle clamp, the length of which is equal to the distance from the 0 point on the hook to its curved end. (5 illustrations.) Ray K. Daily.

Ochoa, R. G. **Anomalous congenital strabismus.** Anales Argentinos de Oft., 1945, v. 6, July-Aug.-Sept., pp. 89-97.

A boy, 10 years of age is described, in whom there were bilateral exophthalmos, esotropia with deviation of the left eye, narrowing of the palpebral fissure of the left eye on adduction, and a weakness of the left lateral rectus. The author reviews several similar cases reported in the literature, and divides them into two groups: those with retraction of the globe on adduction, and those without retraction. When there is retraction there must be a pathologic derangement at the origin of the lateral rectus muscles. When there is no retraction the lesion is probably nuclear. If surgery is contemplated, it should be directed toward attaching a slip of muscle from the superior and inferior rectus muscle to the lateral rectus. (Bibliography.) Edward Saskin.

Pascal, J. I. **Charting diplopia and muscle action.** Amer. Jour. Ophth., 1946, v. 29, August, pp. 1001-1006. (5 figures.)

Scagliono, C. **Miner's nystagmus in the mines of Sardinia.** Rassegna Ital., d'Ottal., 1946, v. 15, no. 1 and 2, p. 20.

In an examination of 30,000 miners in Sardinia the author could not find a single case of miner's nystagmus. He attributes this fact to the conditions under which the laborers work, that is in the erect position, in excellent illumination and good ventilation, and without explosives. All of these factors lessen the psychopathic tendencies which tend to produce miner's nystagmus.

Eugene M. Blake.

5

CONJUNCTIVA

Apin, K. **Trachoma control in Latvia.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 322.

Apin reviews a campaign for the control of trachoma which he carried out in Latvia during the years 1926 to 1940. During that period of 15 years 1029 trachoma patients, or 3 percent of the total number of eye patients were included in this state-wide program. It was found that most patients did not receive effective treatment early enough. The incidence of trachoma was definitely higher in women than in men, possibly because women who take care of trachoma-infected children are more exposed to the infection. Only 36.8 percent of patients were free from complications when treatment was begun. Normal vision in both eyes was found only in 26.6 percent of the patients, and chiefly in the young. Screening of the whole population is difficult or impossible because communities are widely

scattered and the majority of the few available ophthalmologists are in Riga. It is important to discover the disease as early in life as possible. School physicians must examine all pupils for trachoma at least twice a year and industrial employees must be examined at regular intervals. The practicing physicians must check for trachoma all patients who consult them for other ailments. Persons who are exposed to trachoma are watched especially carefully. The names of patients who have trachoma must be reported.

F. Nelson.

Bhat, P. K. **Diphtheritic conjunctivitis complicating septicemia.** The Antiseptic, 1946, v. 42, May, pp. 317-319.

The author describes a boy, eight years of age, who had all the signs of septicemia as well as a bilateral severe conjunctivitis. A thick gray membrane covered the conjunctiva and cornea. No cultures or smears were taken, but there was an almost immediate response to diphtheria antitoxin. Twenty thousand units were injected on three consecutive days. I. E. Gaynon.

Byrn, Willy. **Three cases of hemangioma of the subconjunctiva.** Acta Ophth., 1944, v. 22, pt. 2, pp. 166-175.

Histologically one hemangioma was of the cavernous type, one simple, and the third was untreated and unavailable for microscopic examination. The literature is reviewed and the 67 reported cases analyzed as to the age of observation, localization, and microscopic structure. The data indicate that the neoplasm is mostly congenital; in rare cases trauma is a factor. The place of predilection is the inner canthus and the adjacent bulbar conjunctiva. The conjunctival angiomas have a tendency to grow into the eye muscles and into the orbit and should therefore be removed early. (2 illustrations.)

Ray K. Daily.

Fieandt, Olaf. **A papilloma of the conjunctiva originating in the plica semilunaris.** Acta Ophth., 1944, v. 22, pt. 1, pp. 44-48.

This presumably benign neoplasm, excised from a man 64 years of age, is described clinically and histologically. The variations in the structure of the neoplasm, the difference in the size of the nuclei, and the numerous mitotic figures suggested malignancy. The case illustrates the importance of histologic examination. (3 illustrations.)

Ray K. Daily.

Gartner, S. **Method for biomicroscopic study of the conjunctival blood vessels.** Arch. of Ophth., 1946, v. 35, May, pp. 519-524.

The conjunctival vessels are readily available for study and provide the ophthalmologist with a unique opportunity to learn many of the details of the ocular circulation.

The conjunctival blood vessels can be examined in some detail with the usual slitlamp. However, even with the widest slit there is insufficient light, and much is lost. The slit beam is of little advantage in studying the conjunctival vessels. So much has been written of recent years concerning the value of the sharply focused slit beam of light that it seems to be going backward to remove the slit. However, conditions in the conjunctiva are very different from those in the pupillary zone. In the transparent media of the eye, the narrow focused slit beam of light is a splendid arrangement, while its illumination is near the upper limit of tolerance for most patients. However, on the conjunctiva a wider field of

illumination is advantageous, and higher intensities of light are easily tolerated. With the combination of more light and a larger field, much more becomes visible through the binocular microscope.

The conjunctiva is almost transparent, particularly in older persons, so that the blood vessels are easily seen. The red vessels are arranged in a thin layer against a contrasting white background. The walls of most of these vessels are so thin that they are barely discernible, whereas the blood cells circulating in them are visible. There is a conspicuous variation in many features of the circulation from vessel to vessel. In some there is a swift current, which flows evenly; in others the blood moves slowly and irregularly, and in still others the flow may even stop and be reversed in direction. In a few instances a pulsating movement synchronous with the heartbeat is observed. In some vessels there is a rushing and swirling of a turbulent stream. The aqueous veins, which were so named by Ascher because of their high aqueous content, are readily identified, and their course is easily traced. Delicate lymph channels can be identified in a few instances.

The modification of the slitlamp by which this examination is made possible is described. R. W. Danielson.

Haar, M. **Reiter's disease.** Acta Ophth., 1945, v. 23, pt. 2, pp. 143-150.

In rapid succession an 18-year-old boy developed conjunctivitis, bilateral iritis, prostatitis, and exudative polyarthritis. Gonorrhea was excluded, and the diagnosis of Reiter's disease was made. The eyes made a rapid recovery. The outstanding feature of the case was the pronounced exudation in the eye and joints. Ray K. Daily.

Klar, R. **Corneal involvement in vernal conjunctivitis.** Klin. M. f. Augenh., v. 109, May-June, p. 385. (See Section 6, Cornea and sclera.)

Kove, Simon. **Stevens-Johnson syndrome (eruptive fever with stomatitis and conjunctivitis).** Am. J. M. Sc., 1945, v. 210, Nov., p. 611.

Two cases of Stevens-Johnson syndrome of unknown etiology and characterized by an eruptive fever with membranous stomatitis, purulent conjunctivitis, and severe constitutional reaction are reported. They were encountered within a 2½-week period with no history of contact with each other.

The first patient was treated with sulfadiazine orally in addition to local therapy and recovered completely. The other was desperately ill and was treated with both sulfadiazine and penicillin. After a protracted and extremely stormy course, the patient recovered completely except for a mild chronic residual conjunctivitis and bilateral synechiae.

The effect of either sulfonamide or penicillin therapy cannot be properly evaluated from a review of these two cases.

The etiologic agent may be related to the virus of mumps.

Theodore M. Shapira.

Nižetić, Z. **Swimming pool conjunctivitis or swimmers' (divers') conjunctivitis.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 320.

The term swimming pool conjunctivitis is misleading since it suggests that the infection is only acquired in closed artificial pools, which is not true. Epidemics have been observed in open bathing places such as the Black Sea and Lake Michigan. The author ob-

served six cases in the last two years. He proposes that it would be more appropriate to call the disease swimmers' or divers' conjunctivitis. F. Nelson.

Odegaard, Kristian. **Purulent conjunctivitis with keratitis caused by Neisseria intracellularis (meningococcus).** Acta Ophth., 1944, v. 21, pt. 4, pp. 295-302.

A case of primary meningococcus kerato-conjunctivitis in a hospital maid is reported. Clinically the course resembled gonorrheal ophthalmia. Isolated meningococcus conjunctivitis is rare and some of the reported cases were complicated with meningitis. The diagnosis can only be made from a culture, and it is suggested that some of the cases diagnosed from smears as gonorrheal ophthalmia might have been meningococcus conjunctivitis.

Ray K. Daily.

Osterline, Gote. **An investigation into the presence of lymphatic tissue in the human conjunctiva and its biological and clinical importance.** Acta Ophth., 1944, supplement 23, pp. 77.

The material for this study consisted of the conjunctivas of 92 persons varying in age from the newborn to 81 years. Most of them died within 24 to 48 hours following violent trauma. The conjunctiva was dissected from the tarsus and globe and stained in a solution of gallocyanine, which stains the follicles bluish black so that they can be counted under a binocular loupe. These counts and the histologic data show that the conjunctiva of the newborn is free from follicles. Follicles begin to form in early infancy and reach the maximum of 30 follicles in eyes about the age of eight years. At the age of 15 years their number begins to dwindle and at 25 to 35 years of age their average number is 10. After this age their number varies but little. Up to 15 years of age all subjects had follicles. As the subjects get older one encounters more and more without follicles. In childhood, the follicles are larger and more numerous in the upper conjunctival fold. With the age of the patient they become smaller and more evenly distributed. Microscopically the conjunctival nodules are similar in structure to lymphatic nodules elsewhere in the body. Biologically they are centers of reaction to external irritants. Their task is to participate in the defense of tissue against bacterial and toxic irritants. Correlating the number of follicles with the extent of conjunctival inflammation it appears that follicles are very rarely formed in a conjunctiva which is free from irritation; they were found in declining form in two out of 23 such membranes. Follicle formation is primarily associated with slight or subsiding inflammatory processes, too mild to produce marked clinical symptoms. There is no follicle formation in acute conjunctivitis. These findings indicate that folliculosis of the conjunctiva can not be differentiated into different types etiologically or morphologically, and that in all cases the follicles will eventually disappear spontaneously leaving no scars. (10 illustrations, 4 tables.)

Ray K. Daily.

Pavisic, Z. **Early transplantation of mucous membrane from the mouth and conjunctiva in burns of the eye.** Ophthalmologica, 1944, v. 108, Dec., pp. 297-304.

The author advocates early transplantation of mucous membrane in severe cases of cauterization and burns of the conjunctiva and cornea. When both eyes are affected he uses mucous

membrane from the mouth. When only one eye is damaged, conjunctival tissue from the upper fornix of the undamaged eye can be used if the burn is not too extensive. In several patients early transplantation only prevented a more marked symblepharon and did not prevent corneal leucoma, but in several others normal vision was preserved. The latter was especially true after acid burns. Max Hirschfelder.

Poulsen, A. G. **A case of melanocarcinoma conjunctivae.** Acta. Ophth., 1945, v. 23, pt. 2, pp. 151-160.

The literature is reviewed and a case reported in a 23-year-old woman. The growth recurred twice and microscopic examination after the third excision revealed the growth to be a melanocarcinoma. The clinical as well as the histological differential diagnosis between a benign and malignant naevus is difficult, and all conjunctival naevi should be considered as an intermediate stage between normal tissue and actual tumor tissue. Suggestive of transition into malignancy is the location at the temporal limbus, increased pigmentation and growth, vascularization from peripheral vessels, adhesion at the base, inflammatory symptoms, ciliary pain, recurrence after excision, and occasionally iritis. (Photomicrograph.)
Ray K. Daily.

Radnót, M. **Bacteriologic findings in gonorrheal conjunctivitis treated with sulfa drugs.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 344.

When sulfamid drugs are used in the treatment of ophthalmoblennorrhea, gonococci often disappear from the conjunctival sac in a few days. Occasionally gonococci can be found for a long time after clinical cure. Certain precautions are imperative to prevent recurrence and transmission of the disease by these carriers. Before discharge three smears taken at intervals of 48 hours should be negative. Gram staining should be used to avoid confusion with staphylococci which often resemble diplococci, although it is believed that some gonococci become Gram-positive during the administration of sulfa drugs. The final bacteriological examination should be carried out after the disappearance of clinical symptoms and after the patient is free from sulfa drugs. (References.)
F. Nelson.

Skydsgaard, Henning. **Polyarthritis urethritica simplex with eye symptoms.** Acta Ophth., 1943, v. 21, pts. 1-2, pp. 107-118. (See Section 17, Systemic diseases and parasites.)

Sorsby, Arnold. **Ophthalmia neonatorum in England, 1844-1944.** Sight-saving Review, 1945, v. 15, Winter, pp. 187-196.

In 1844 more than 30 percent of all blind children lost their sight through ophthalmia neonatorum; in 1928 it was 28.5 percent and in 1944 not more than 9.2 percent. Three factors that brought about the decline are the Crede technique, compulsory notification of the disease, and the use of sulfonamides. The latter has been replaced by penicillin. A solution containing 2500 units per c.c. is recommended at half hour intervals although in the last seventy-two patients at White Oak hospital one drop of penicillin was instilled every minute. The formation of pus stopped in one half hour and the residual catarrhal conjunctivitis disappeared in two or three days. Ophthalmia neonatorum is not synonymous with gonococcal ophthalmia. Of 737 cases, 180 were caused by gonococcus, 271 by the vari-

ous types of staphylococcus, 119 cases by bacilli, and in 126 cases no organisms were found. Fifteen percent of all cases appeared to be caused by a virus.

I. E. Gaynon.

Ulrich, K. **Chemo-therapautic treatment of gonorrhea.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 347.

Thirteen infants with gonoblennorrhea neonatorum were given the sulfa drug orsulon. In 11 infants the eyes recovered completely in three to five days. One infant developed slight cyanosis. In another, a very feeble baby who could not tolerate the drug, the process was not influenced greatly. Recovery was slow and complications occurred in infants who were not breastfed or were given only small amounts of mothers' milk. Only one of the 13 infants developed a corneal infiltration, which healed rapidly. Local treatment is unnecessary. (References.)

F. Nelson.

Vanýsek, J. **Conjunctivo-urethro-synovial syndrome of Fiessinger and Leroy or Reiter's disease.** Časopis Lékařů Českých, 1946, v. 85, March 15, pp. 343-347.

Several cases of conjunctivitis with arthritis and urethritis were observed during an outbreak of infectious keratitis. This disease, called Reiter's disease, usually follows an attack of diarrhea. Reiter claimed that he was successful in isolating a spirochete, which he called Spirochete forans, from the secretions. Fiessinger and Leroy, however, stated that the disease is a sequel of bacillary dysentery. The author observed seven patients with conjunctivitis and superficial punctate keratitis, in three of whom there was also iridocyclitis. Urethritis and arthritis were present in all patients. The illness started after diarrhea. It lasted three weeks and longer. No gonococci and no spirochetes were found. While the bacteriologic diagnosis of bacillary dysentery was not established, the author believes that in the patients observed by him the syndrome was a complication of dysentery, which was prevalent at that time.

O. Felsenfeld.

Wain, Harry. **Ophthalmia Neonatorum—A historical résumé and present status in the United States.** Sight-Saving Review, 1945, v. 15, Winter, pp. 196-202.

The author discusses ophthalmia neonatorum from the point of view of gonorrhea. He describes the disease, its history in the United States, the Crede technique, and makes a plea for the eradication of the disease in the mother before the birth of the child. The incidence of blindness due to ophthalmia neonatorum has dropped from 30 to 2.4 percent. I. E. Gaynon.

6

CORNEA AND SCLERA

Becker, F. **The etiology and therapy of epidemic keratitis.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 412.

In the treatment of epidemic keratitis (nummularis) the use of Greifswald dye solution and subsequent treatment with 0.5 to 1-percent salicylic acid solution and 10-percent zinc oxide ointment yielded very gratifying results. The same ointment was also administered successfully in a case of a severe post-traumatic herpes of the cornea. F. Nelson.

Bedell, A. J. **Epidermoid carcinoma of the cornea.** Amer. Jour. Ophth., 1946, v. 29, July, pp. 864-866. (5 figures.)

Chamberlain, W. P. and Boles, D. J. **Edema of cornea precipitated by quinacrine (atabrine).** Arch. of Ophth., 1946, v. 35, Feb. pp. 120-134.

Six cases of corneal edema following the use of quinacrine (atabrine) were observed in the Southwest Pacific area. Four of the patients are described in considerable detail. Each patient had been taking protective doses of quinacrine, from 0.1 gm. to 0.2 gm. of the drug, for several weeks before the onset of symptoms. Visual acuity was variable. There was diffuse haziness of the corneas due to evenly dispersed punctate, superficial opacities. Withdrawal of the drug resulted in gradual clearing of the opacities. Resumption of the use of the drug resulted in a reappearance of the edema. All four of the cases studied intensively showed some liver damage, and one of the patients died of hepatic necrosis.

John C. Long.

Friede, R. **The nature of congenital corneal degeneration.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 390.

Dystrophy of the cornea is a disease that is essentially congenital but becomes manifest during postnatal life.

Bückler described three readily distinguishable types. Friede observed a number of cases of congenital corneal dystrophy over a period of 20 years and investigated the heredity of the process of the various types. The type of heredity is recessive. In some patients remissions of more than 10 years duration occurred between the thirtieth and fiftieth year of life. The first opacities were always found near Bowman's membrane and the anterior layers of the stroma. The middle and posterior layers at the corneal periphery became involved later. Exceptions to this rule were rare. Most details concerning nutrition of the cornea are not yet known. The intake of nutrient material may take place through the limbus and its capillaries, through the posterior vitreous membrane and its endothelium and through the anterior vitreous membrane and its epithelium. Lesions of the anterior as well as the posterior barrier must lead to swelling and eventually to clouding of the corneal stroma. The water content in the stroma is kept constant though it is exposed to the aqueous barriers, but only if these structures are intact and their function is not impaired. The chemical structures in endothelium and epithelium on the one hand and in the stroma on the other are quite different. The epithelium forms an acid covering over the alkaline stroma. Bowman's membrane and its epithelium probably serve as filter. The functions of the vitreous membranes have not been investigated sufficiently but much may be surmised. In the congenital corneal dystrophies the most serious change takes place in the anterior vitreous membrane. A disturbance of filtration in that membrane occurs. The involvement of Bowman's membrane seems to be the primary process and that of Descemet's membrane the secondary. The other vitreous membranes of the eye never participate in the pathological process. It is probable that the disease is a local process rather than a general one. Friede is inclined to believe that all three types of congenital corneal dystrophy are caused by the same agent, namely a disturbance of the metabolism of Bowman's membrane and epithelium. The differences of clinical appearance and development of the various opacities may be caused by congenital differences in the structure of the stroma. The hyaline of which the

opacities in dystrophic corneas consist is probably caused by a chronic retention of certain substances which eventually leads to disintegration of the tissues and to permanent opacities in epithelium, vitreous membrane and stroma. (Bibliography.) F. Nelson.

Friedenwald, J. S., Hughes, W. F., Jr., and Herrmann, H. **Acid burns of the eye.** Arch. of Ophth., 1946, v. 35, Feb., pp. 98-108.

The following acids, in buffered and non-buffered solutions, were tested on the rabbit cornea: hydrochloric, trichloracetic, metaphosphoric, sulfosalicylic, picric, tungstic, and tannic. Clinical reactions produced by solutions of these acids on the rabbit cornea were studied over a pH range of 1 to 9.

Acid burns of the eye are essentially nonprogressive, and late relapses are uncommon. The severity of the lesion produced is directly related to the protein affinity of the anion. Anions with high protein affinity and protein-precipitating ability produce corneal lesions at a higher pH than anions with low protein affinity. Large anions with high protein-precipitating ability show poor penetration through the corneal epithelium and poor diffusibility in the stroma. It is suggested that the characteristics of acid burns of the cornea may be explained by the precipitation and denaturation of the proteins of the cornea. (7 photomicrographs.)

John C. Long.

Fieandt, Olaf. **A histologically examined case of corneal transplantation.** Acta Ophth., 194, v. 22, pt. 1, pp. 36-43.

An eye with vision reduced to hand movements as a result of parenchymatous keratitis was treated by a corneal transplantation. The eye subsequently developed an anterior chamber cyst, and was enucleated. The histologic picture of the transplanted cornea supports the claim of those who consider the transplanted cornea as a permanent transplant and not merely a scaffold for regenerative processes, as is claimed by Salzer and Löhlein. The transplanted area contained all the corneal layers. Bowman's membrane, present in the transplant, was partially absent in the surrounding cornea and completely absent at the margin of the transplant. Descemet's membrane was thinner in the transplant. The literature is reviewed. (5 illustrations.)

Ray K. Daily.

Gallenga, R. and Rossi, A. **Early relief of corneal affections with plesiotherapy (contact radiation).** Rassegna Ital. d'Ottal., 1946, v. 15, no. 1 and 2, p. 7.

The authors report excellent results in ulcerous keratitis of various types, pannus, recent corneal opacities, and especially in herpetic keratitis. The optimum dose of radiation was 400 r, with a tension of 60 kVm and a 0.5 mm. copper filter. Working with 3 Ma at a focal distance of 6 cm., 100 r was administered per minute with the Gorla Siama instrument. The treatment is given daily for one week in acute inflammations, and the course is repeated in subacute and chronic conditions.

The best results were obtained in herpetic keratitis where corneal sensibility returned rapidly, proliferation of superficial vessels was checked, and congestion decreased.

Eugene M. Blake.

Grosz, Stefan. **A new remedy for the treatment of phlyctenular keratitis.** Acta Ophth., 1944, v. 22, pt. 3, pp. 275-280.

The author found a 15-percent sodium irgamid (N-Dimethylacroyl-

Sulfamid) ointment to be non-irritating and well tolerated in phlyctenular conjunctivitis in children. It is particularly indicated in eyes which do not tolerate yellow oxide of mercury, and can be combined with the internal administration of iodine. Its action is attributed to vasoconstriction. Ray K. Daily.

Holt, M. and Cogan, D. G. **The cornea.** Arch. of Ophth., 1946, v. 35, March, pp. 292-298.

In connection with recent studies of the permeability and other properties of the excised cornea, Holt and Cogan thought that measurements of electrical impedance might be expected to give additional pertinent information. It is now generally accepted that the impedance of biologic tissues is directly related to their ionic permeability. In the same way that measurements of impedence of solutions of pure electrolytes may be considered to measure (aside from concentration effects) the ability of the ions to diffuse through the medium, measurements of impedance of the cornea may be considered to give a measure of the ability of the ions to move through this tissue.

The authors used the corneas of beef eyes and came to the following conclusions.

Electrical impedance of the excised cornea is considerable as long as the epithelium is present. The impedance of the stroma alone is slight. So far as impedance is an index of ionic permeability, this means that the epithelium offers considerable resistance to the passage of ions, whereas the stroma offers a resistance little more than that offered by an equivalent volume of isotonic solution of sodium chloride.

The corneal epithelium is an even more effective semipermeable membrane than previous chemical measurements have shown it to be.

The impedance of the epithelium of the excised cornea is irreversibly decreased by bathing the cornea in a 25-percent solution of sodium chloride; it is unaffected by a 0.9-percent solutions of sodium chloride, calcium chloride, and sodium nitrate, and it is reversibly increased by a 10-percent solution of atropine sulfate, by a 4-percent solution of cocaine hydrochloride, and, especially, by solutions in which the cation is the potassium ion.

R. W. Danielson.

Jancke, G. **Cibazol treatment of keratoconjunctivitis nummularis epidemica and of other eye diseases.** Klin. M. f. Augenh., 1943, v. 109, May-June, p. 314.

Jancke reports most satisfactory results in the treatment of keratoconjunctivitis nummularis with 10-percent cibazol eye ointment twice daily. When the disease is severe it is necessary to give scopolamine regularly, and when extreme, one has to resort to intensive peroral administration of cibazol. Other infectious eye diseases such as corneal ulcers, dacryophlegmon, orbital phlegmon, and erysipelas respond well to intensive therapy. It can also be applied as an adjuvant in intraocular infections. It seems that trachoma can be cured by oral administration of cibazol alone. Combined with customary mechanical methods this is the shortest possible type of treatment of trachoma. (References.)

F. Nelson.

Kiehle, F. A. **Scleromalacia.** Amer. Jour. Ophth., 1946, v. 29, July, pp. 862-863. (References.)

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
904 Carew Tower, Cincinnati 2

News items should reach the editor by the twelfth of the month

DEATHS

Dr. Benjamin George Dyer, Kalamazoo, Michigan, died May 15, 1946, aged 80 years.

Dr. Alan Fesch Knisely, Lima, Ohio, died June 12, 1946, aged 87 years.

Dr. John Alexander McCaw, Denver, Colorado, died March 28, 1946, aged 79 years.

Dr. Howard Wilber Peirce, Detroit, Michigan, died April 17, 1946, aged 65 years.

MISCELLANEOUS

Dr. Placidus J. Leinfelder, professor of ophthalmology, Iowa State University, was a member of the faculty committee which, after several months' study, recommended a two-year experimental plan for faculty compensation in the College of Medicine, Iowa City.

The plan, recently approved by the Iowa State Board of Education, adopts a salary schedule for the various professional ranks in medicine. Private clinical practice was authorized, with percentage limits based on individual salaries. Fees from private patients will be credited to the clinical department giving the service. From this income, the faculty doctors will be paid the additional stipulated percentage of their basic salaries. Funds remaining will be used for departmental equipment and scientific programs. Professors desiring to serve on a full-time basis will, as in the past, be permitted to do so.

Preliminary steps were put into effect immediately, according to the report published in the Iowa City Citizen of July 25th, and the plan will be in full force by July 1, 1947. After a two-year trial, the plan will be reviewed by the university authorities in consultation with the faculty of medicine.

The Army Institute of Pathology is in the process of undergoing a considerable expansion and change of organization. It will still continue to be the Institute of Pathology for the United States Army, but it will also function for the Veterans' Bureau and play an expanded role in the activities of the civilian profession.

On request of Major Gen. Norman T. Kirk, Surgeon General of the Army, the committee on pathology of the National Research Council, Division of Medical Sciences, late in 1945, prepared a report on the future development of the Institute. The report has been approved by the Surgeon General and by the War Department.

The essential recommendations in this report are: (1) that a new building of adequate size be constructed; (2) that the Institute be organized in four divisions—Department of Pathology, Army Medical Illustration Service, Army Medical Museum, and American Registry of Pathology—each headed by a competent specialist; (3) that the staff of the Institute be drawn from both the commissioned ranks of the Army and from the civilian professions; (4) that a comprehensive educational and training program be undertaken; (5) that the vast store of material at the Institute be used for research; (6) that the services in pathology in the Veterans' hospitals be centralized at the Institute.

The American Registry of Pathology founded in 1922 thus is, and will continue to be, an integral part of the Army Institute of Pathology. There were, on January 1, 1946, over 43,000 cases registered. To effectuate the new plans as they relate to the Registry, the National Research Council, Division of Medical Sciences, appointed a committee on the American Registry of Pathology. The members of the committee are Howard T. Karsner, chairman, Cleveland; Col. J. E. Ash, Washington; Brig. Gen. R. Callender, Washington; Col. Baldwin Lucké, Philadelphia; Robert A. Moore, Saint Louis; Benjamin Rones, Washington; A. R. Shands, Jr., Wilmington; and Henry A. Swanson, Washington.

At the present time there are 14 registries as parts of the American Registry of Pathology. These include Registry of Ophthalmic Pathology, established in 1922, sponsored by the American Academy of Ophthalmology and Otolaryngology; Lymphatic Tumor Registry, established in 1925, sponsored by the American Association of Pathologists and Bacteriologists; Bladder Tumor Registry, established in 1927, Kidney Tumor Registry, established in 1940, and Prostatic Tumor Registry, established in 1943, sponsored by the American Urological Association; Registry of Dental and Oral Pathology, established in 1933, sponsored by the American Dental Association; Registry of Otolaryngological Pathology, established in 1935, sponsored by the American Academy of Ophthalmology and Otolaryngology; General Tumor Registry, established in 1937, sponsored by the American Society of Clinical Pathologists; Registry of Dermal Pathology, established in 1938, sponsored by the American Academy of Dermatology and Syphilogy; Chest Tumor Registry,

established in 1942, sponsored by the American Society of Thoracic Surgeons; Registry of Neuropathology, established in 1943, sponsored by the American Association of Neuropathologists; Registry of Orthopedic Pathology, established in 1943, sponsored by the American Academy of Orthopedic Surgeons; Registry of Veterinary Pathology, established in 1944, sponsored by the American Veterinary Medical Association; and Registry of Gerontology, established in 1945, sponsored by the Gerontological Society, Inc.

Plans for additional registries are under consideration. A professional scientific society wishing to sponsor a registry should communicate with the Director, Army Institute of Pathology, 7th Street and Independence Avenue, S.W., Washington 25, D.C. The society appoints a committee to work with the Director in supervision of the activities of the Registry, and makes an annual contribution to the budget which is administered by the National Academy of Sciences.

All specimens in the Registry are available for review and research by competent investigators. Sets of slides and accompanying syllabuses on special fields are available for loan to the civilian professions and to officers in the Federal services. Physicians, dentists, and veterinarians are urged to send unusual specimens together with an abstract of the history to the Registry. The contributor receives a report on each specimen and is asked to keep the Registry informed of the follow-up on the patient.

Many diseases are so rare that any one individual or even the staff of any one hospital or clinic has a limited opportunity to study certain conditions and lesions. Conclusions in science must be based on not one, but many observations. Therefore, it is desirable to organize and support central agencies for the collection and filing of histories, specimens, and follow-up studies.

With the reorganization of the Army Institute of Pathology to be completed during 1946 and 1947, a full-time scientific director of the American Registry of Pathology will be appointed and sufficient clerks and technicians will be available to assure adequate use of the registries for diagnosis, research, training of young men, and education of the professions.

The American Registry of Pathology deserves support from the civilian professions in terms of contributions of materials by individuals and sponsorship of registries by societies.

The Ophthalmological Study Council is planning another course of lectures (this time with some laboratory work) to be given this winter, November 2nd to January 15th in St. Petersburg, Florida, by a very exceptional group of lecturers from all over the United States. Like the first course, this one will be devoted to the basic subjects of Ophthalmology: Anatomy, Histology, Embryology, Heredity, Physiology, Biochemistry, Optics, Physiological optics, Pathology, Histopathology (including laboratory work with microscopes), Bacteriology, Refraction (theoretical and practical), Motility, Neuro-ophthalmology, Slitlamp (theoretical and practical in four sections), Surgical principles, Relations to general diseases, and Glaucoma (from all points of view). There will be over 360 hours of instruction. The fee is $300.

Arrangements can be made to take special subjects either singly, or two or three at a time, when they are given simultaneously in alternating periods. For instance: Biochemistry by Kinsey, Optics by Lancaster, and Visual physiology by Linksz can be taken during 10 days. Glaucoma by Chandler and Medical ophthalmology by Wagener can be taken during one week. Motility by Burian and Refraction by Beach, Regan, and Lancaster can be taken during another 10 days. Pathology with microscopes, and laboratory work on Optics and on Physiology can be taken from December 21st through December 31st. Fees depend on the number of periods; the average is about $40 per week.

First class hotel accommodations are from $4 per day, single, to $6 per day, double. Round trip rates by coach are very low. For example: Boston to St. Petersburg and return costs $60.82 plus tax.

The 20th annual spring graduate course in ophthalmology and otolaryngology will be held at the Gill Memorial Eye, Ear, and Throat Hospital, Roanoke, Virginia, April 7 to 12, 1947.

Societies

The program for the Association of Military Surgeons, Eye, Ear, Nose and Throat panel discussion, October 11, 1946, at the English Room, Statler Hotel, Detroit, Michigan, follows:

Morning, 9 o'clock

Comdr. A. Duane Beam (MC), U.S.N.R., Detroit, Michigan. "Traumatic injuries of the eyes and their repair."

Lt. Col. James N. Greear (MC), A.U.S., Washington, D.C. "Rehabilitation of the blind."

Lt. Col. Gilbert C. Struble (MC), A.U.S., Valley Forge General Hospital, Phoenixville, Pennsylvania. "Repair of eye injuries" (Movie).

Lt. Col. E. L. Shiflett (MC), A.U.S., William Beaumont General Hospital, El Paso, Texas. "X-Ray reconstruction of orbit as an aid to surgical reconstruction."

Lt. Col. Ben. H. Senturia (MC), A.U.S., Saint Louis, Missouri. "Ear plugs for the prevention of deafness."

Lt. Col. Edmund P. Fowler (MC), A.U.S., New York, New York. "Irradiation of the eustachian tubes."

Afternoon, 2 o'clock

Lt. Col. Mercer G. Lynch (MC), A.U.S., New Orleans, Louisiana. "Laryngeal injuries and their repair."

Capt. Francis L. Lederer (MC), U.S.N.R., Chicago, Illinois. "Rehabilitation of the deaf in the Navy."

Lt. Col. Frank D. Lathrop (MC), A.U.S., Boston, Massachusetts. "Facial nerve repair due to war injury."

Dr. Julius Lempert, New York, New York (by invitation). "Lempert fenestra novovalis operation for the restoration of practical serviceable hearing in clinical otosclerosis" (motion picture of technique).

Honorary chairmen: Maj. Gen. Norman T. Kirk (MC), U.S.A., and Vice Adm. Ross T. McIntyre (MC), U.S.N.

Personals

At the exhibit of the American Physicians Literary Guild held in San Francisco in conjunction with the A.M.A. convention, Dr. Joseph I. Pascal was awarded first prize for a humorous essay "If you must wear glasses—wear invisibles."

Dr. James C. Strong, recently released from Service, announces the opening of his office, 617 Majestic Building, Denver 2, Colorado.

Dr. Alston Callahan, professor of ophthalmology, Medical College of Alabama, announces the opening of his office, 908 South Twentieth Street, Birmingham, Alabama.

Dr. John C. Cunningham, 49 South Winooski Avenue, Burlington, Vermont, has been named chairman of the department of ophthalmology at the College of Medicine, University of Vermont, Burlington.

On November 21, 1946, Dr. Algernon B. Reese will deliver the deSchweinitz Lecture before the Section on Ophthalmology of the College of Physicians, Philadelphia.

Dr. Adalbert Fuchs of Vienna wishes to let his friends and colleagues in the United States know that he and Mrs. Fuchs have accepted employment with UNRRA and that, until further notice, his address will be: Headquarters, UNRRA, Shanghai, China.

ERRATA

The obituary of Dr. James Watson White which was published in the August issue of the Journal was prepared and written by Dr. Harold Whaley Brown, an associate of the late Dr. White.